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Phospho Sulfonic Acid Catalyzed Synthesis of Benzimidazole, Benzoxazole and Quinoxaline Derivatives under Green Solvent at Ambient Temperature

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Abstract

Phospho sulfonic acid (PSA) synthesized as an environmentally safe and efficient solid acid catalyst, and it used for the synthesis of several 2-disubstituted benzimidazoles, 2-substituted benzoxazoles, and 2-substituted quinoxalines in ethanol as a green solvent at ambient temperature is described. (i) A very simple, green and efficient procedure for the synthesis of benzimidazole and also benzoxazole derivatives comprising the reaction of corresponding ortho-phenylenediamine or ortho-aminophenol with various aromatic aldehydes in absolute ethanol at ambient temperature is described. (ii) The direct condensation of various 1,2-diamines and carbonyl compounds in absolute ethanol at ambient temperature has been described to the synthesis of quinoxaline derivatives as biologically interesting compounds. Additionally, PSA is reused repeatedly for six reaction cycles without any evidence loss of activity. This green procedure offers significant advantages in terms of its simplicity, reusable strategy for the efficient synthesis of benzimidazole derivatives, the elimination of corrosive liquid acids, short reaction time, high product yields, and simple preparation of the catalyst.

Keywords: Benzimidazoles; Benzoxazoles; Quinoxalines; Phospho sulfonic acid; Brønsted acid.

Introduction

Application of solid acids in organic transformation has an important role, because, solid acids have many advantages such as decreased reactor and plant corrosion problems, simplicity in handling, and more environmentally safe disposal in different chemical processes [1]. Also, wastes and by-products can be minimized or avoided by using solid acids in developing cleaner synthesis routes. A large number of

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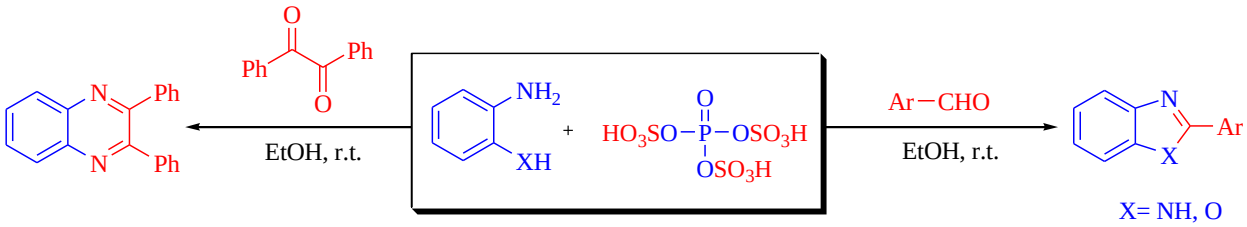


Scheme 1. PSA catalysed synthesis of benzimidazoles, benzoxazoles, and quinoxalines derivatives.

benzimidazole and benzoxazole derivatives are found in a variety of natural products and wide range of biologically active compound, especially including anti ulcerative, antihypertensive, antiviral, antimicrobial, anticancer properties (colon cancer therapies), and as kinase inhibitors [2-3]. Also it used as an important pharmacophore in modern drug discovery and exhibit significant activity against several viruses such as HIV, human cytomegalovirus (HCMV), Herpes (HSV-1), RNA, and influenza [4]. Typically, to date several synthetic methods, involves the treatment of *ortho*-phenylenediamine either with carboxylic acids under strongly acidic conditions or aldehydes under oxidative have been investigated for the synthesis of benzimidazole derivatives [5-12]. Also, *ortho*-nitroaniline has evolved to include the synthesis of benzimidazoles via one step reduction and cyclisation [13]. In the first method, the drastic reaction conditions employed often as low yields, side reactions, and requires high temperatures. Which the reaction of *ortho*-phenylenediamin with various aldehydes under oxidative is the most common procedure. 1,2-Disubstituted benzimidazoles have been synthesized using a variety of catalysts or reagents such as $TiCl_4$ [14], PPA [15], $SOCl_2/SiO_2$ [16], L-Praline [17], Zeolite [18], H_2O_2–HCl [19], $Sc(OTf)_3$ [20], $In(OTf)_3$ [21], $Yb(OTf)_3$ [22], sulfamic acid [23], *N*-halosuccinamide (X = Cl, Br, I) [24], polyaniline-sulfate [25], pyridinium-p-toluenesulfonate [26], $I_2/KI/K_2CO_3/H_2O$ [27], ionic liquids [28], sulfur/ultrasonic [29], and (bromodimethyl)sulfonium bromide [30]. However, literature survey demonstrated that reported methods have suffered drawbacks such as long reaction time, usage of expensive and corrosive reagent, used hazardous solvent such as organic solvent as compared to ethanol and ethanol:water mixture, higher catalyst loading, not reusable, low yield, and relatively higher temperature conditions. The preparation of quinoxaline, its derivatives have great importance in organic synthesis. Quinoxaline derivatives are very important class of nitrogen-containing compounds and have been shown to possess a broad spectrum of biological activities such as anti bacterial, antifungal, anti inflammatory, anti depressant, anti cancer, anthelmintic agents, and antitumor drugs [31]. Also quinoxaline is a part of the chemical structures of various antibiotics such as Echinomycin, Levomycin and Actinoleutin are known to inhibit the growth of Gram-positive bacteria and are also active against various transplantable tumors [32]. Besides these, they have been also used as building blocks for the synthesis of organic semiconductors [33], wide application in dyes [34], and also applied for the extraction of metal cations [35]. Recently, PSA was found to be an effective solid acid catalyst for the synthesis of indazolo[1,2-b]-phthalazinetriones [36] was reported by Kiasat *et al.* and as a promising solid acid catalyst for acid-catalyzed reactions, such as preparation of acylals [37], synthesis of bis-(4-hydroxycoumarin-3-yl) methanes [38], and synthesis of 14-dibenzo[a,j]xanthenes and 1,8-dioxo-octahydro-xanthenes [39]. Phospho sulfonic acid as an environmentally friendly and heterogeneous solid acid catalysts that offer several advantages such as safe, excellent solubility in water, long catalytic life, cleaner reactions in comparison to conventional catalysts (less waste production), high catalytic activities, thermal stability and recyclability, readily prepared and inexpensive, can conveniently be handled and removed from the reaction mixture. In continuation of our studies on the solid acids [40-49], we prepared PSA as a reusable and efficient catalyst led to formation of high yield and short reaction time of benzimidazole, benzoxazole and quinoxaline derivatives under green solvent at ambient temperature (Scheme 1).

Materials and Methods

General

All the solvents and reagents were purchased from Aldrich and Merck with high-grade quality and used without any purification. Melting points were measured by using capillary tubes on an electrothermal digital apparatus and are uncorrected. Products were separated and purified by different chromatographic techniques and were identified by the comparison of their NMR with those reported for the authentic samples. NMR

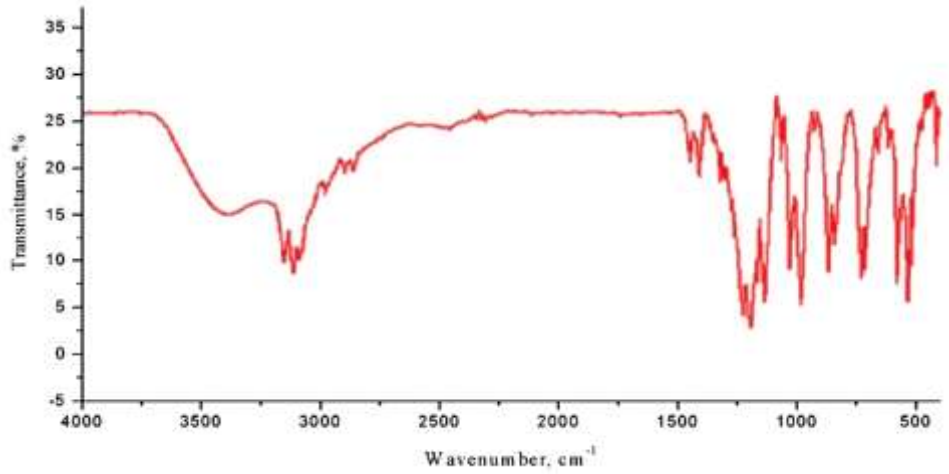


Figure 1. The FT-IR spectrum of phospho sulfonic acid (KBr disc).

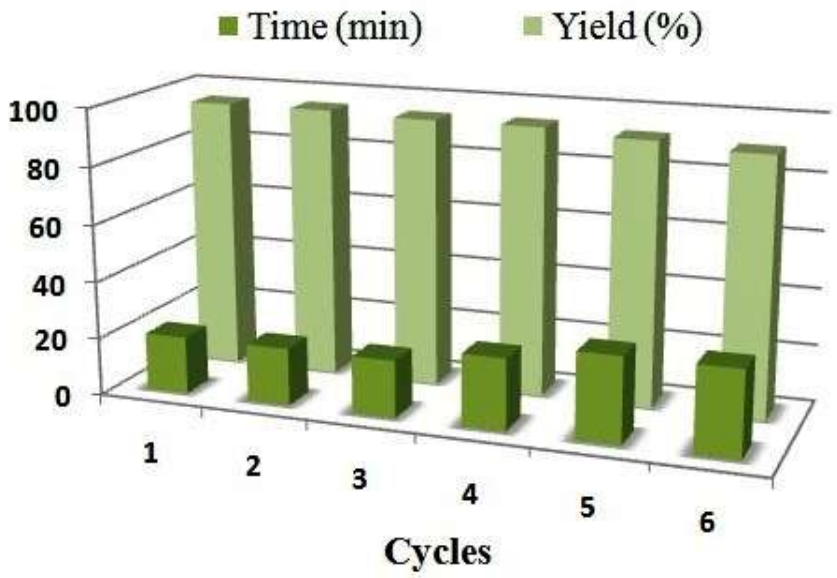


Figure 2. Catalyst reusability.

Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) with the residual solvent as internal reference (DMSO-d_6, δ 2.50 ppm for ^{1}H NMR and δ 39.5 ppm for ^{13}C NMR; CD_3OD, δ 3.31 ppm for ^{1}H NMR and δ 49.0 ppm for ^{13}C NMR; $CDCl_3$, δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR). NMR Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. The reaction was monitored by TLC using on 0.25 mm E-Merck silica gel 60 F254 precoated plates, which were visualized with UV light.

Preparation of phospho sulfonic acid

A 100 ml suction flask was equipped with a constant pressure dropping funnel. The gas outlet was connected to a vacuum system through adsorbing solution (water) and alkali trap. Diammonium hydrogen phosphate (4 g, 30 mmol) was charged into the flask and chlorosulfonic acid (10.48g, ca. 6 mL, 90 mmol) in CH_2Cl_2 (10 mL) was added dropwise over a period of 45-60 min at ambient temperature. After completion of the addition, the mixture was shaken for 2 h, while the residual HCl was eliminated by suction. Then the mixture was washed with CH_2Cl_2 (2×5 mL) to remove the unreacted chlorosulfonic acid (Fig. 2). Finally, a solid white

powder was (solid acid) obtained and it is a free flowing powder that can be stored at ambient temperature for several months without losing its catalytic potentiality [36].

General procedure for synthesis of benzimidazole and benzoxazole derivative (Table 3)

In a 50 ml round bottom flask, *ortho*-phenylenediamine/*ortho*-aminophenol (1 mmol), benzaldehyde (1 mmol) were dissolved in 10 ml of EtOH was stirred magnetically at ambient temperature. To this solution, PSA (5 mol%) was added and stirred for the required time at ambient temperature for a certain time (Table 3). The progress of reaction was monitored by TLC. On completion of reaction, the catalyst was recovered by filtration and filtrate was extracted with ethyl acetate (2×10 ml). By evaporation of the solvent, the crude product was recrystallized from hot ethanol to obtain the pure compound.

General procedure for synthesis of quinoxaline derivative (Table 5)

In a 50 ml round bottom flask, carbonyl compounds (1 mmol), benzaldehyde (1 mmol) were dissolved in 10 ml of EtOH was stirred magnetically at ambient temperature. To this solution, PSA (5 mol%) was added and stirred for the required time at ambient temperature for a certain time (Table 5). The progress of reaction was monitored by TLC. On completion of reaction, the catalyst was recovered by filtration and filtrate was extracted with chloroform (2×10 ml). By evaporation of the solvent, the crude product was recrystallized from hot ethanol to obtain the pure compound.

2-Phenyl-1H-benzo[d]imidazole (Entry 1)

Mp 295-296 °C (Lit. 292−294 °C) [50]. ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 12.87 (broad s, 1H), 8.20-8.16 (m, 2H), 7.60-7.46 (m, 5H), 7.23-7.18 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 116.0, 124.0, 127.9, 130.2, 131.1, 131.5, 140.3, 153.5.

2-(p-Tolyl)-1H-benzo[d]imidazole (Entry 2)

Mp 276−277 °C (Lit. 275-277 °C) [50]. ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 12.79 (s, 1H, -NH), 8.05-8.08 (d, J = 10.2 Hz, 2H), 7.56-7.59 (m, 2H), 7.34-7.36 (d, J = 10.2 Hz, 2H), 7.17-7.21 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) δ 20.9, 114.9, 121.9, 126.3, 127.4, 129.4, 139.5, 151.3.

2-(4-Methoxyphenyl)-1H-benzo[d]imidazole (Entry 3)

Mp 223-224 °C (Lit. mp 222−225 °C) [50]. ^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 7.99-8.02 (m, 2H), 7.54-7.57 (m, 2H), 7.20-7.22 (m, 2H), 7.03-7.08 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD): δ (ppm) δ 56.0, 115.6, 123.5, 123.7, 129.5, 153.6, 163.0.

2-(4-Chlorophenyl)-1H-benzo[d]imidazole (Entry 5)

Mp 289-290 °C (Lit. mp 289-291°C) [50]. ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 13.13 (broad s, 1H), 8.23 (d, J = 8.5 Hz, 2H), 7.64-7.58 (m, 2H), 7.34-7.18 (m, 4H). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 115.8, 115.9, 124.2, 129.3, 129.7, 130.3, 137.3, 152.1.

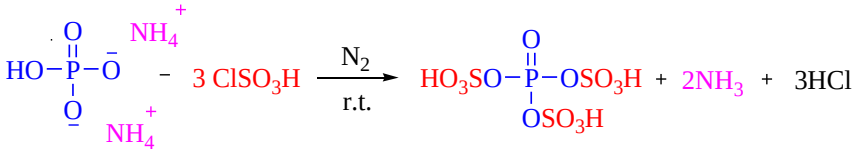
2-Phenylbenzo[d]oxazole (Entry 11)

Mp 103-104 °C (Lit. mp 102−103 °C) [50]. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.21-8.27 (m, 2H), 7.75-7.79 (m, 1H), 7.48-7.58 (m, 4H), 7.31-7.36 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.8, 120.2, 124.7, 125.3, 127.3, 127.8, 129.1, 131.7, 142.3, 150.9, 163.2.

Results and Discussion

Phospho sulfonic acid as a solid acid and heterogeneous catalyst was easily prepared by the simple mixing of diammonium hydrogen phosphate and neat chlorosulfonic acid under N_2 atmosphere with 83% yield at ambient temperature. This reaction is very easy and clean, because the by-products of the reaction are HCl and NH_3 gases, which are immediately evolved from the reaction vessel (Scheme 2).

One of the informative techniques for an investigation of catalyst formation is FT-IR spectroscopy. Thus, the structure of the catalyst was characterized by FT-IR spectroscopy using the KBr disc technique (Fig. 1). As seen in Fig 1, the FT-IR spectrum of PSA showed absorption bands at 1422 (S=O,



Scheme 2. Preparation of the phospho sulfonic acid.

Table 1. Comparison of activity of some solid acid catalysts for the synthesis of 2-Phenylbenzimidazole of *ortho*-phenylenediamine with benzaldehyde at ambient temperature.

Entry	Catalyst	Time (min)	Yield (%)[a]
1	None	24 h[b]	NR[b]
2	Boric acid	120	50
3	Citric acid	120	55
4	SESA	120	65
5	Silicagel	120	NR[b]
6	MTSA	120	78
7	PSA	80	88

[a] Isolated yields. [b] No reaction.

Table 2. The influence of different solvents (10 ml) on the reaction benzaldehyde (1 mmol) with *ortho*-phenylenediamine (1 mmol) in the Presence of PSA (5 mol%) at ambient temperature.

Entry	Solvent	Time (min)	Yield (%)[a]
1	CH_2Cl_2	100	65
2	$CHCl_3$	150	74
3	CH_3CN	150	71
4	$(CH_3)_2CO$	150	33
5	EtOH	20	95
6	Ethyl acetate	120	18
7	H_2O	90	76
8	THF	150	16

[a] Isolated yields.

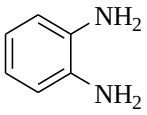
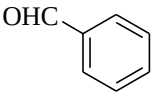
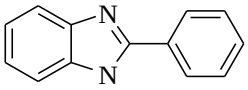
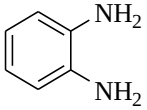
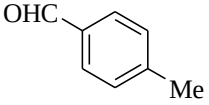
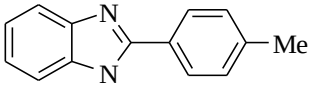
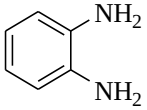
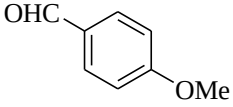
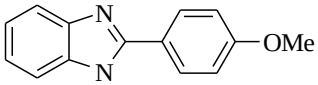
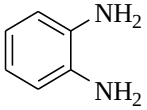
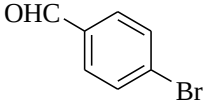
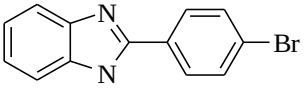
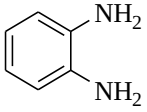
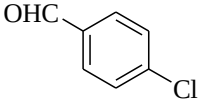
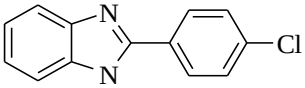
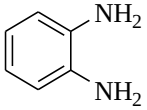
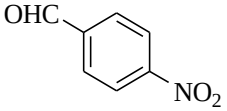
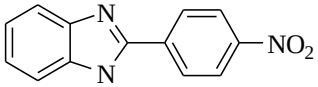
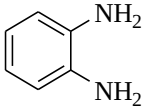
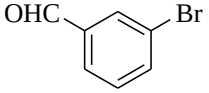
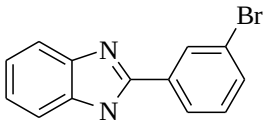
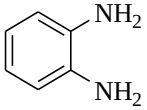
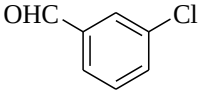
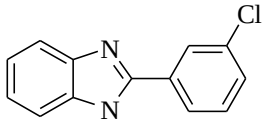
asymmetric stretching), 1210 (S=O, symmetric stretching) and also for S–O showed a one absorption bands stretching mode at 628 cm^{-1}. Also, on the other hand the broad peak showed around 3412 cm^{-1} corresponds to the O-H stretching.

In the first step, to evaluate the catalytic activity of various Brønsted acids for the preparation of benzimidazole derivatives, a model reaction of *ortho*-phenylenediamine (1 mmol), and benzaldehydes (1 mmol) at ambient temperatures and in the presence of variable catalyst loadings was examined, that the results are summarized in Table 1. It was found that in the absence of catalyst, no corresponding 2-Phenylbenzimidazole even after 24 hour (Table 1, entry 1). It can be seen that Brønsted acids such as boric acid (Table 1, entry 2), citric acid (Table 1, entry 3), and [2-(ulfooxy)ethyl]sulfamic acid (Table 1, entry 4) are less efficient. Remarkably, it is also clearly seen from these data that no yield of the corresponding 2-Phenylbenzimidazole was obtained when amorphous silicagel were employed as catalysts (Table 1, entry 5). Interestingly, the yield was dramatically increased using melamine trisulfonic acid (Table 1, entries 6). Best result was obtained, when that the reaction was performed in the presence 5 mol% of phospho sulfonic acid, it proceeded rapidly to give the desired product (Table 1, entry 7).

In the second step, the effect of various aprotic and protic solvents such dichloromethane, chloroform, acetonitrile, acetone, ethanol, ethyl acetate, water, and tetrahydrofuran in the model reaction was investigated and the results are summarized in Table 2. As Table 2 indicates, excellent yields and short reaction time were obtained, when the reaction was carried in ethanol. Thus, to show the generality of this method, the optimized conditions used for the synthesis of benzimidazole derivatives and all results are summarized in Table 3.

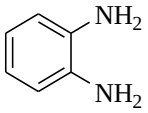
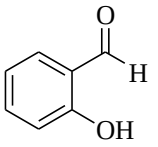
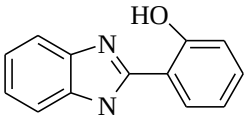
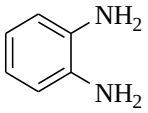
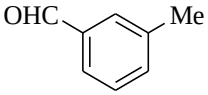
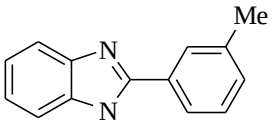
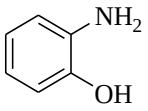
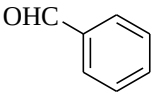
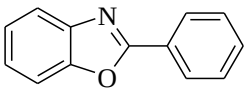
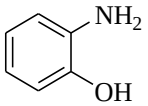
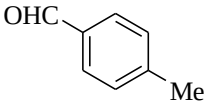
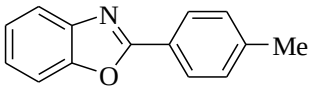
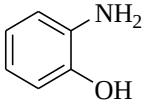
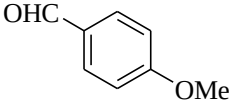
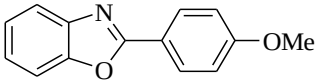
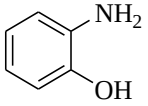
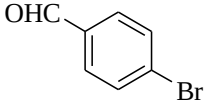
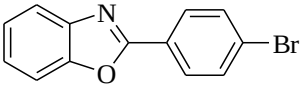
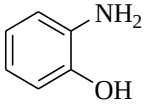
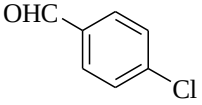
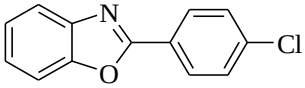
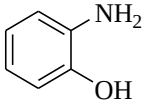
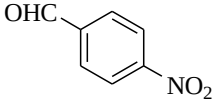
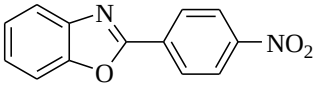
As shown in Table 3, to the reaction of *ortho*-phenylenediamine to benzaldehyde (Table 3, entry 1), 4-methylbenzaldehyde (Table 3, entry 2), 4-methoxybenzaldehyde (Table 3, entry 3), 4-bromobenzaldehyde (Table 3, entry 4), 4-chlorobenzaldehyde (Table 3, entry 5), 4-nitrobenzaldehyde (Table 3, entry 6), 3-methylbenzaldehyde (Table 3, entry 10), afforded the

Table 3. Reaction of *ortho*-phenylenediamine and *ortho*-aminophenol with various aromatic aldehydes in the presence of PSA.

Entry	Diamines	Aldehyde	Product	Time (min)	Yield (%)[a]
1				20	95
2				20	92
3				20	90
4				10	95
5				10	95
6				15	90
7				25	81
8				25	80

products in excellent yields and high purities in the short reaction time. 3-Bromobenzaldehyde (Table 3, entry 7), 3-chlorobenzaldehyde (Table 3, entry 8), and 2-hydroxybenzaldehyde (Table 3, entry 9) reacted with *ortho*-phenylenediamine in short reaction time and good yield. Of the reaction to *ortho*-aminophenol with 4-bromobenzaldehyde (Table 3, entry 14), 4-chlorobenzaldehyde (Table 3, entry 15), afforded the

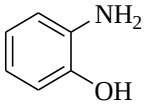
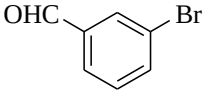
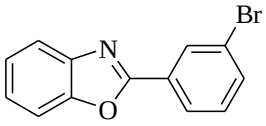
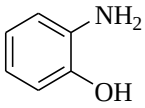
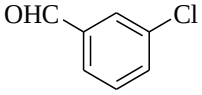
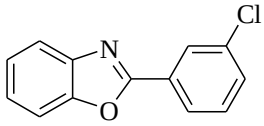
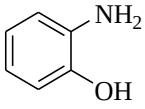
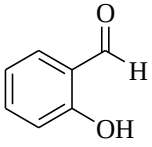
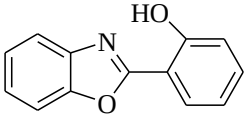
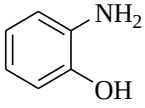
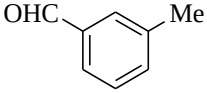
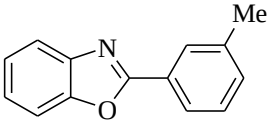
Table 3. Cntd

9				30	85
10				15	90
11				25	94
12				30	90
13				40	88
14				15	85
15				15	85
16				30	85

products in the good yields and short reaction time. 3-Bromobenzaldehyde (Table 3, entry 17), 3-chlorobenzaldehyde (Table 3, entry 18) reacted to *ortho*-aminophenol at the time of a slightly longer and acceptable yield. According to the results reported in Table 3, this method is effective for the preparation of benzimidazole and benzoxazole derivatives.

In order to show the merit of the PSA with recently reported protocols such some homogeneous and heterogeneous catalysts for the synthesis of benzimidazoles derivatives has been presented in Table 4. The results clearly show that, some catalysts such

Table 3. Cntd

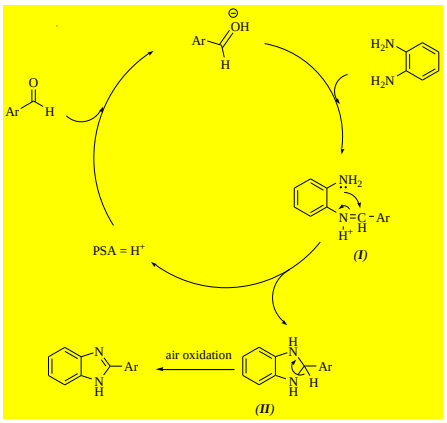
17				30	78
18				30	75
19				35	88
20				30	90

[a] Isolated yields.

Zn^{2+}-K10-clay, ENPFR, CAN, glycerol, Cu-np/SiO_2, Iron(III)sulfate-silica, PEG 400, and silica sulfuric acid for completion of the reaction requires longer reaction time. In the other hand, some catalysts such glycerol, I_2, and silica sulfuric acid reacted in the low yield. Also some procedures used from reflux conditions and higher temperature for the completion of the reaction. As you can be seen, our procedure was simpler, more efficient, without the need for temperature and toxic solvents, and low amount of the catalyst, that show PSA is a powerful catalyst for the synthesis benzimidazole derivatives, that without doubt, our procedure a clean and environmentally friendly reaction.

Another advantage of the our methodology is the reusability of the catalyst (Fig. 2). The reusability of the catalyst, was examined using the condensation reaction of benzaldehyde with *ortho*-phenylenediamine under the optimized conditions. After the reaction completion, the mixture was filtered and also the remaining was washed with ethyl acetate, and the catalyst reused in the next reaction. This process was repeated to six runs and no appreciable yield decrease was observed. In six runs, the yields of product were 95%, 95%, 94%, 94%, 92% and 90%, respectively, that the difference between the PSA content of the fresh and reused catalyst (6^{th} run) is only 5% which verifies that the activity of the catalyst remained unchanged throughout these six runs.

A suggested mechanism for the preparation of benzimidazole and benzoxazole derivatives are reported in Scheme 3. Initially, involve H-bond formation between the catalyst and aldehyde and then the reaction between an aldehyde and a diamine (*ortho*-



Scheme 3. Proposed mechanism for the synthesis of benzimidazoles.

Table 4. Comparison of PSA with the reported catalysts for the benzimidazole derivatives.

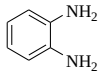
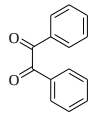
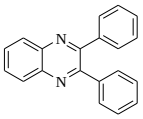
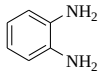
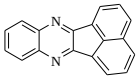
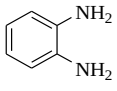
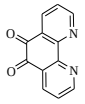
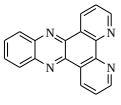
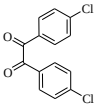
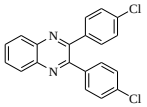
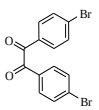
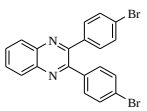
Entry	Catalyst/ solvent/ temperature	Time (h)	Yield (%)[f]	[Ref]
1	$Zn(OAc)_2$/ solvent-free/ ambient temperature	10[e]	92	[52]
2	Zn^{2+}-K10-clay[a]/ H_2O:CH_3OH/ ambient temperature	24	94	[53]
3	ENPFR[b]/ EtOH/ reflux	3	88	[54]
4	*p*-TsOH/ DMF/ 80 °C	10[e]	85	[55]
5	CAN/ PEG[c]/ 50 °C	2	98	[56]
6	Glycerol/ H_2O/ 90 °C	2	75	[57]
7	I_2/ K_2CO_3, H_2O/ ambient temperature	45[e]	75	[58]
8	Cu-np/SiO_2[d]/ CH_3OH/ ambient temperature	4	93	[59]
9	Iron(III)sulfate-silica/ solvent-free/ 30 °C	2	89	[60]
10	PEG 400/ solvent-free/ 110 °C	6	90	[61]
11	Silica sulfuric acid/ EtOH/ ambient temperature	1.5	75	[62]
12	Silica sulfuric acid/ water/ ambient temperature	2	71	[62]
13	PSA/ EtOH/ ambient temperature	20[e]	95	-[g]

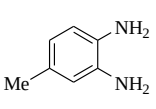
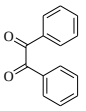
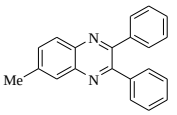
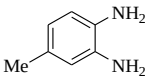
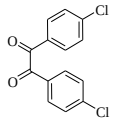
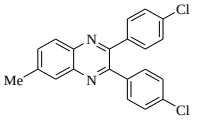
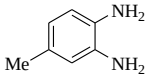
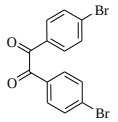
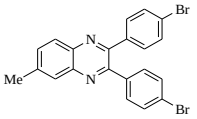
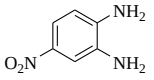
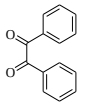
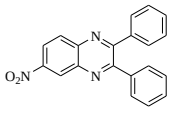
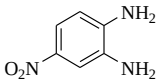
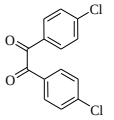
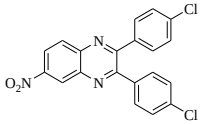
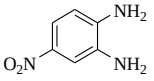
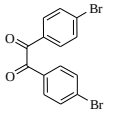
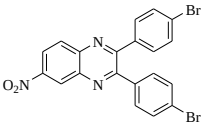
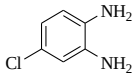
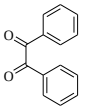
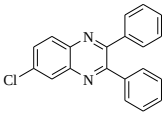
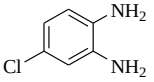
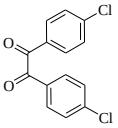
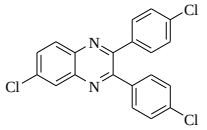
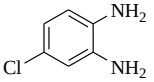
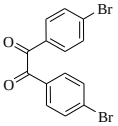
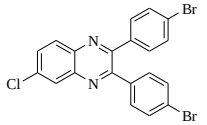
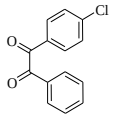
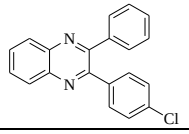
[a] Zinc chloride-exchanged K10-montmorillonite. [b] Epoxidized novolac phenol formaldehyde resin modified using sulfanic acid. [c] Polyethylene glycol. [d] Silica supported nano-copper (II) oxide. [e] In minute. [f] Isolated yields. [g] Our work.

phenylenediamine and *ortho*-aminophenol) leads to the formation of structure (I) and The next step, attack by the second amino group on C=N double bond facilitates the formation of hydro benzimidazole (II) which undergoes subsequent air oxidation to give the desired benzimidazole as the final product.

To establish the generality and scope of our procedure, in another study, we developed a highly efficient and facile procedure for the quinoxaline derivatives from various 1,2-diketones and 1,2-diamines in the presence of PSA (5 mol%) in EtOH as a green media at ambient temperature to afford quinoxaline derivatives as biologically interesting compounds (Table 5).

Table 5. Reaction of *ortho*-phenylenediamine with various 1,2-diketones in the presence of PSA.

Entry	Diamines	Diketone	Product	Time (min)	Yield (%)[a]
1				15	95
2				15	91
3				10	90
4				30	88
5				25	91

6				15	93
7				20	91
8				20	95
9				30	89
10				30	89
11				30	91
12				20	90
13				20	90
14				20	94
15				15	93

[a]Isolated yields.

As shown in Table 5, a series of 1,2-diamines (electron-withdrawing and electron-donating) reacted with various 1,2-dicarbonyls in green solvent at ambient temperature to afford a wide range of quinoxaline derivatives, mostly in excellent yields and short reaction time. Benzil (Table 5, entry 1), acenaphthylene-1,2-

dione (Table 5, entry 2), and 1,10-phenanthroline-5,6-dione (Table 5, entry 3) reacted with *ortho*-phenylenediamine in short reaction time and excellent yield. When electron-withdrawing and electron-donating 1,2-diamines such as 4-chlorobenzene-1,2-diamine, 4-nitrobenzene-1,2-diamine, and 4-methylbenzene-1,2-diamine was used for the reaction with various 1,2-diketone such as benzil, acenaphthylene-1,2-dione, 1,2-bis(4-chlorophenyl)ethane-1,2-dione, 1,2-bis(4-bromophenyl)ethane-1,2-dione, the desired products were also obtained with excellent yield and short reaction time (Table 5, entries 6-14). On the other hand, we also examined the reaction of unsymmetrical 1,2-diketons such as 1-(4-chlorophenyl)-2-phenylethane-1,2-dione with *ortho*-phenylenediamine (Table 5, entry 15). Similarly, the corresponding products were obtained with excellent yield and short reaction time.

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