Research on Chemical Intermediates
https://doi.org/10.1007/s11164-021-04450-6

One-pot synthesis of multicomponent pyrazole-4-carbonitrile derivatives under solvent-free condition by using engineered polyvinyl alcohol catalyst

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Received: 20 January 2021 / Accepted: 25 March 2021

Abstract

Heterocyclic chemistry has fascinated the researchers owing to its wide range of applications in various chemical fields. With this perspective, herein we present an environmentally benign procedure for the synthesis of pyrazole and its derivatives through multicomponent reaction by using SPVA as a heterogeneous acid catalyst. The synthesis protocol of SPVA catalyst includes functionalization of polyvinyl alcohol by sulfonic acid groups. The synthesized SPVA catalyst was then subjected to several characterization techniques to confirm its formation and study its physicochemical properties. The SPVA catalyst was then tested for its activity toward a multicomponent reaction of aromatic aldehyde, malononitrile and phenyl hydrazine. The SPVA catalyst with sufficient acidic sites displayed appreciable catalytic performance yielding 89% of the desired pyrazole product under ambient reaction conditions. The SPVA catalyst showed recyclability up to the sixth cycle without considerable loss in its activity. Furthermore, we made an effort to demonstrate the plausible mechanistic pathway for the SPVA-catalyzed pyrazole synthesis reaction. Interestingly, the present synthetic approach could effectively produce pyrazole products with high yields in the absence of base and solvent and in short reaction time making it a green and sustainable process.

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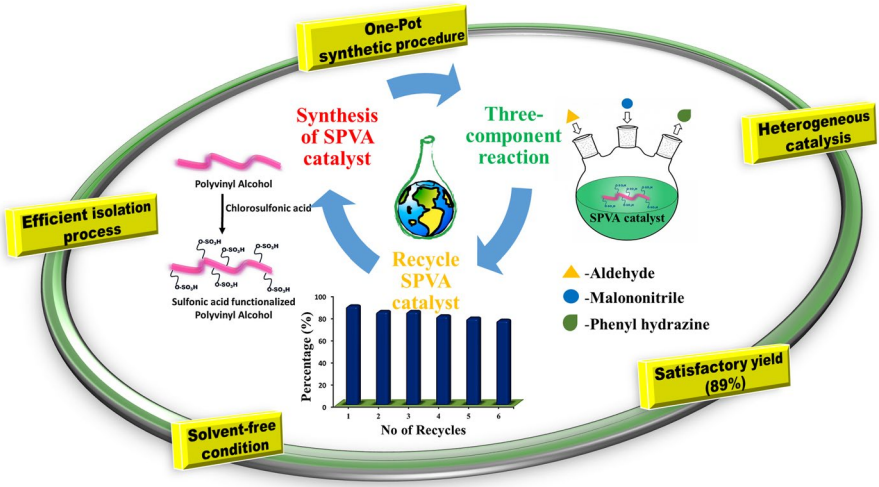
Published online: 05 April 2021

Graphic abstract



Keywords Sulfonic acid-functionalized polyvinyl alcohol (SPVA) · Bronsted acidity · Pyrazole synthesis · Three-component reaction · Aromatic aldehyde · Malononitrile · Phenyl hydrazine

Introduction

The chemistry of heterocycles has gained tremendous attention of researchers worldwide in the recent years due to their relevance in diverse field [1, 2]. Precisely, heterocyclic compounds hold an important place in medicinal chemistry that show potent biological activity [2, 3]. They also can take part in different types of cross-coupling reactions [4, 5]. Few heterocycles are used in polymer and supra-molecular chemistry, cosmetic industry and food industry, while some have properties of liquid crystal [6]. Owing to the several advantages, researchers have been focusing on the synthesis of several heterocyclic molecules by diverse synthetic procedures [5, 7–12].

Among several heterocyclic compounds, pyrazole which is a five-membered ring containing two nitrogen atoms has emerged as a significant class of N-heterocycles showing pharmaceutical and biological activities such as antimalarial, antibacterial, anti-parasitic, anti-depressant, anticancer and anti-inflammatory activities [13]. Pyrazole derivatives also find the application as herbicides and insecticides and act as ligands in complexes [14]. Traditionally, substituted pyrazoles can be synthesized by the condensation reaction between hydrazines and 1,3-dicarbonyl compounds or their 1,3-dielectrophile equivalents [14]. Additionally, intermolecular [3 + 2] cycloadditions of 1,3-dipoles to alkynes can also lead to the formation of substituted pyrazoles [14]. However, as time progressed, more efficient synthetic protocols have

been developed, which can result in enhanced regioselectivity. Multicomponent reaction (MCR) is one of the efficient methods that have been practiced currently to synthesize pyrazole and its derivatives [5, 15, 16]. The multicomponent reaction offers certain merits over traditional methods such as reduction in the required energy, requiring less time, reduction in cost and formation of lesser or no side products [5, 7, 8].

The most certain way for the preparation of the 5-aminopyrazole-4-carbonitriles moiety is a multicomponent reaction of aromatic aldehydes, hydrazine derivatives and malononitrile [17, 18]. Numerous types of catalysts and reagents such as molecular iodine, ionic liquids, nanoparticles, piperidine, $Cu(OAc)_2$, CuO/ZrO_2, graphene oxide–TiO_2, piperidinium acetate, palladium and copper, alum, cerium (IV) ammonium nitrate have been explored for this reaction [19–29]. However, several drawbacks were encountered in the reported literature work that needs to be resolved. Precisely, use of toxic reagents, harsh reaction conditions and strong acidic or basic medium constrain their use in large-scale applications. Additionally, the expensive chemicals and catalysts, tedious synthesis procedure and low yields of product or time-consuming reaction further restricted their application at industrial scale. Specifically, metals are lethal, costly, rare and not environmentally friendly, which make metal-based catalysts non-sustainable for their application in organic transformations. However, the significant importance of pyrazoles and its derivatives in medicine field has persistently fascinated the search for environmentally friendly and inexpensive catalytic systems. Therefore, there is need for search of greener catalysts without metals. The efficacy of metal-free catalysts can somewhat overcome few disadvantages of metal catalysts. Additionally, in some cases, metal-free catalysis offers certain advantages, such as unique performance, recyclability and substrate tolerance [30, 31]. With respect to this, the use of biodegradable polymers such as polyvinyl alcohol, poly glycolic acid, polyvinylpyrrolidone and polyethylene glycol by functionalizing its surface with several acidic groups has received high attention by organic chemists [32–34]. Among the above-mentioned polymers, polyvinyl alcohol (PVA) polymer has been a choice of interest as it is considered highly productive due to its biodegradable quality and water solubility even at high temperatures along with the properties such as presence of –OH groups, low cost, high thermal stability and low toxicity [35, 36].

Therefore, in this perspective of pursuing environmentally benign, Bronsted acidic catalyst for the heterocycles synthesis, specifically pyrazoles derivatives, we synthesized sulfonic acid-functionalized polyvinyl alcohol (SPVA) by functionalization of PVA surface with Bronsted acidic group by using a reported procedure. The SPVA catalyst was characterized by several characterization techniques which revealed the presence of acidic sites in the catalyst. Further, SPVA was tested for its catalytic activity toward a one-pot synthesis of pyrazole-4-carbonitrile derivatives by reacting aromatic aldehydes, hydrazine derivatives and malononitrile. We observed that the SPVA catalyst displayed admirable yield of 89% toward pyrazole product in solvent-free condition. Additionally, the SPVA catalyst demonstrated appreciable tolerance to the aldehyde with different functional groups. The SPVA catalyst also presented recyclability performance up to six recycles without considerable loss in its catalytic performance. Therefore, SPVA can be considered as an

efficient Bronsted acidic heterogeneous catalyst for synthesis of pyrazole derivatives offering several merits which makes the present protocol sustainable enough for scale-up process.

Materials and methods

Materials

Polyvinyl alcohol (PVA; 19% hydrolyzed) with average molecular weight of 85,000–124,000 g mol^{-1} was purchased from Sigma-Aldrich, India. 1,2-Dichloroethane (MW: 98.96 g mol^{-1}) with 99.8% purity and chlorosulfonic acid (MW: 116.53 g mol^{-1}) with 99% purity were also supplied by Sigma-Aldrich, India. Methanol solvent was obtained from local dealer and used as such without further purification. The starting materials used for the synthesis of pyrazole and its derivatives were also purchased from Sigma-Aldrich. The purity of all the purchase chemicals was 99.9%. The melting point of compounds was carried out in an open capillary and is uncorrected. The synthesized compounds were purified by recrystallization in ethyl alcohol and characterized by ^{1}HNMR and ^{13}CNMR.

Synthesis of PVA functionalized with sulfonic acid (SPVA)

PVA was functionalized with sulfonic acid by employing a simple synthesis method reported elsewhere [32]. Precisely, 100 mL 1,2-dichloro ethane was taken in a 500-mL two-necked round-bottom (R.B) flask and 10 g of PVA was added into it. A reflux condenser was attached to the two-necked R.B flask. The reaction mixture was agitated at R.T for 2 h. Later, 45 mL of chlorosulfonic acid was added dropwise slowly to the suspension of PVA in 1,2-dichloroethane using a syringe pump. The reaction was run for half an hour at room temperature, and then, the temperature was elevated to 90 °C and maintained for an hour. After completion of reaction time, the reaction mixture was naturally cooled to room temperature. Subsequently, the reaction was placed in an ice bath in order to bring the temperature down to 0 °C. At 0 °C, on addition of 100 mL methanol to this reaction mixture we observed the formation of black solid. The resultant solid was filtered and washed with distilled water and methanol alternatively for at least four times. The obtained solid was overnight dried at 110 °C in an oven.

Catalyst characterization methods

The formation and crystalline nature of the samples were confirmed using X-ray diffraction patterns (XRD). A Rigaku diffraction Ultima-IV X-ray diffractometer (Rigaku Corporation, Japan) was used to analyze the samples. Ni-filtered Cu Kα radiation ($\lambda = 1.5406$ Å) was employed, and the samples were run with a scan rate of 20 min^{-1} at a 2θ range of 5–80° at 30 kV and 15 mA. FTIR spectra of prepared samples were recorded using a Perkin Elmer FTIR spectrometer (Spectrum Two).

KBr disc method was employed for the obtaining the FTIR spectra. The morphology, presence of different elements and their uniform distribution in the samples were examined using a field emission scanning electron microscope (FESEM) coupled with EDX (JEOL Model-JSM7). Determination of the acidic sites in the sample was analyzed by temperature-programmed desorption (TPD) technique by using an indigenous instrument containing a quartz tube reactor attached to a six-port valve coupled to a thermal conductivity detector (TCD). For acidic sites, NH_3 was employed as a probe molecule.

General procedure for synthesis of pyrazole

A solution of substituted aromatic aldehyde (1 mmol) and malononitrile (1 mmol) was taken in the reactor. Catalytic quantity of sulfonic acid-functionalized polyvinyl alcohol (SPVA) was then added to the solution. The resultant reaction mixture was refluxed at 90 °C, till solid precipitate was obtained. As soon as the precipitate was obtained, phenyl hydrazine (1 mmol) was added to the solution and further refluxed for certain period of time. The reaction progress was examined by thin-layer chromatography (TLC) in the pet ether: ethyl acetate solvent system. On completion of reaction, the reaction mixture was poured in ice-cold water. The obtained crude solid product was filtered, washed with cold water and dried under vacuum. The product was further recrystallized by pure hot ethyl alcohol to obtain the pure product. Although all the synthesized compounds are well reported, the characterization details of compounds are described in the following.

Chemical characterization data of the synthesized products

5-Amino-1,3-diphenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 1): (yield—89%) (m.p—158–159).

^{1}H NMR (400 MHz, $CDCl_3$): δppm 6.83 (d, 1H), 7.10(dd, 2H), 7.10–7.30(m, 5H),

7.35(d, 1H), 7.66(S, 2H), 7.69(d, 1H). ^{13}C NMR (400 MHz $CDCl_3$): δppm 75.6, 115.8, 123.4, 126.8, 127.4, 128.5, 129.2, 129.4, 131.2, 139.7, 145.4, 153.2.

5-Amino-3-(2-methoxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 2: (yield—82%) (m.p—130–131).

^{1}H NMR ($CDCl_3$): *δ*ppm 3.81(s, 3H), 6.82–7.07(s, 4H), 7.23–7.60(s, 5H), 7.84(s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 55.38, 77.4, 112.0, 114.0, 119.1, 120.0, 127.6, 129.2, 129.3, 136.2, 138, 145, 159.

5-amino-1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazole-4-carbonitrile (Table 3, compound 3): (yield—74%) (m.p—128–130).

Cream color solid.

^{1}H NMR (400 MHz, $CDCl_3$): δppm 3.83(s, 6H), 3.92(s, 3H), 6.90(d, 2H, ArH), 7.19–7.28(m, 5H, ArH), 7.67(s, 2H). ^{13}C NMR (400 MHz $CDCl_3$): δppm 56.1, 60.9, 77.6, 103.2, 112.9, 120.3, 127.9, 129.3,131, 137.1, 139, 145.1, 153.4.

5-Amino-3-(2-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3,compound 4): (yield—68%) (m.p—159).

^{1}H NMR (400 MHz, $CDCl_3$): δppm 6.80–7.10(m, 4H), 7.20–7.76(m, 5H), 7.83(s, NH_2), 10.84(s, 1H). ^{13}C NMR (400 MHz $CDCl_3$): δppm 76.7, 116.6, 119.0, 120.2, 123.4, 126.3, 128, 130.2, 131.5, 140.8, 144.1, 156.4.

5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3,compound 5): (yield—82%) (m.p—128–129).

^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.00–7.50(m, 5H, Ar–H), 7.50–7.98(m, 4H), 7.72(s, 2H). ^{13}C NMR (400 MHz, $CDCl_3$): δ ppm 77.0, 113.2, 121.1, 126.9, 128, 128.2, 129.2.129.3, 139.3, 145.4,153.

5-Amino-3-(2, 4-dichlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 6): (yield—84%) (m.p—162–163).

^{1}H NMR ($CDCl_3$): *δ*ppm 7.40–7.60(s, 5H), 7.45–8.10(s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 74.4, 116, 123.4, 127.4, 128.5, 129.6, 130.2, 130.6, 130.9, 133.8, 135.5, 136.2, 148.6, 153.5.

5-Amino-3-(2, 6-dichlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 7): (yield—80%) (m.p—158–159).

^{1}H NMR ($CDCl_3$): *δ* 7.40–7.65(s, 3H), 7.45–7.68(s, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 74.4, 123.4, 126.2, 127.4, 129.4, 130.5, 132.3, 133.8, 139.8, 148.9, 154.

5-Amino-3-(2-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 8): (yield—89%) (m.p—160–161).

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 6.82(t, 1H), 7.11(d, 2H), 7.25(t, 2H), 7.49(t, 1H), 7.71(t, 1H), 7.97(d, 1H), 8.16(d, 1H), 8.25(s, 1H), 10.89(s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): d 112.9, 120.2, 124.9, 126.8, 127.4, 128.6, 129.7, 130.3, 131.1, 133.6, 144.9, 147.2.

5-amino-3-(4-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 9): (yield—86%).

Red solid, (m.p—161–162) 0.175–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δppm 6.95(d, 1H), 7.15–7.26(m, 5H), 7.78(s, NH_2), 7.98(d, 1H), 8.23(dd, 2H). ^{13}C NMR (400 MHz, $CDCl_3$): δppm 112.60, 119.81, 124.43, 125.76, 126.96, 127.52, 129.01, 130.51, 130.74, 132.81, 144.54, 146.59.

5-Amino-3-(4-hydroxy-3-methoxy phenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, compound 10): (yield—78%) (m.p—156–158).

^{1}H NMR ($CDCl_3$): *δ* 3.86(s, 3H), 7.40–7.60(s, 3H), 7.45–7.68(s, 5H), 5.35(s, 1H), 7.3(s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) 56.1, 77.2, 107.1, 109.1, 112.0, 114.6, 121.0, 128.2, 126.2, 129.9, 137.1, 148, 153.

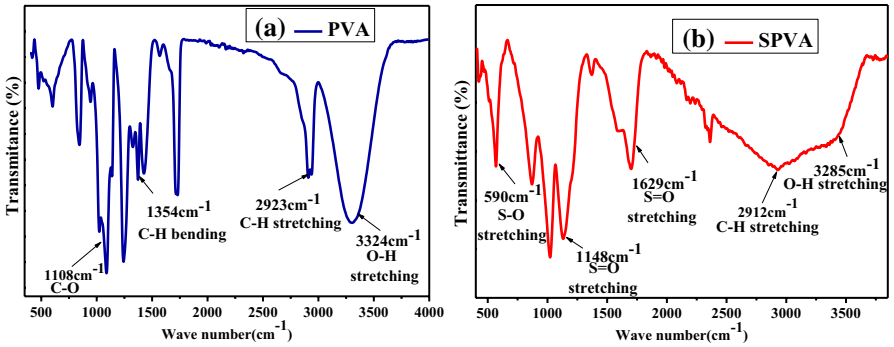


Fig. 1 FTIR spectrum of **a** PVA and **b** SPVA

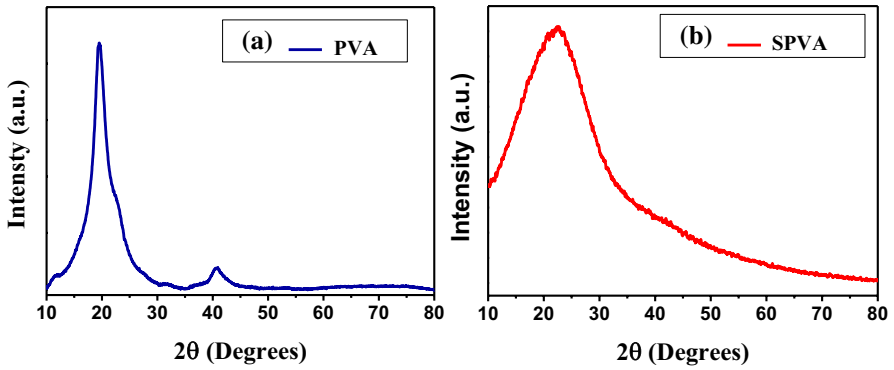


Fig. 2 XRD pattern of **a** PVA and **b** SPVA

Results and discussion

Catalyst characterization

FTIR analysis

FTIR characterization technique was performed to explore the presence of functional groups present in the PVA and SPVA samples and therefore confirm successful functionalization of PVA to form SPVA. The IR spectrum of pristine PVA and SPVA is presented in Fig. 1a, b. The FTIR spectrum of pristine PVA displayed a broad and intense peak centered at 3325 cm^{-1} that corresponds to the stretching frequency of O–H bond (Fig. 1a) [33]. This particular O–H stretching vibration can be attributed to the presence of hydroxyl groups of PVA bonded to hydrogen [33]. Further, the C–H bond in the PVA structure was confirmed by the presence of peaks at 2925 cm^{-1} and 1350 cm^{-1} which correspond to the stretching and bending vibrations of C–H bond [33]. After functionalization of PVA with sulfonic acid, FTIR analysis of resultant SPVA was performed that

displayed a broad band centered at 3285 cm^{-1} (Fig. 2b). The peak corresponds to the stretching vibration of O–H group which signified the presence of hydroxyl group. However, the intensity of –OH peak in SPVA was reduced and appeared significantly broader in comparison to PVA. The reason could be attributed to the intra-molecular hydrogen bonding present in SPVA molecule [34].

Further, the presence of C–H network in the SPVA matrix was confirmed by the occurrence of asymmetric stretching peak at 2912 cm^{-1}. Peaks at 1629 cm^{-1} and 1148 cm^{-1} ascended due to the O=S=O asymmetric stretching vibration [37]. Additionally, a sharp peak in the finger print region centered at 590 cm^{-1} could be ascribed to the stretching vibration of S–O bond [37]. The existence of O=S=O and S–O bond in the FTIR spectrum of SPVA thus confirmed the successful formation of SPVA.

XRD analysis

XRD analysis of pristine PVA and synthesized SPVA catalyst was performed to obtain information on the crystalline nature and confirm the formation of sulfonic acid-functionalized PVA. The XRD pattern of pristine PVA (Fig. 2a) displayed diffraction peaks at 2θ values of 11.2, 19.5 and 41.8° which correspond to the characteristic peaks of standard PVA [32]. The peaks in XRD pattern of PVA clearly reflect the crystalline nature of PVA. The reason can be the presence of stacked molecular series of polymer caused due to the strong interfaces between the side-chain –OH groups [32]. After functionalization process, certain changes were observed in the XRD pattern of resultant SPVA (Fig. 2b). A broad peak was observed at the 2θ value of 22.3°, which signified destruction of crystalline nature and stacked chain of polymer in SPVA due to the functionalization of PVA with sulfonic acid group [32]. The interaction of -OH groups with sulfonic acid groups inhibited intermolecular bonding and thus resulted in the formation of amorphous SPVA [32]. Further, we could observe that a peak at $2\theta = 41.8°$ in the XRD graph of PVA diminished in the XRD pattern of SPVA due to broadening of peak.

FESEM and elemental (EDX) and mapping analysis

FESEM analysis of pristine PVA and sulfonic acid-functionalized PVA was performed to investigate the morphological changes occurring in PVA after functionalization with sulfonic acid. The results of PVA and SPVA obtained are shown in Fig. 3a–f, g–l. Precisely, FESEM images of pristine PVA displayed clusters of small particles (Fig. 3a–f). These irregular clusters altogether demonstrated agglomerated morphology. As could be observed from the magnified images, the surface of pristine PVA appears smooth. Further, on performing FESEM analysis of PVA after functionalizing it with sulfonic acid not much change was observed in the morphology of SPVA (Fig. 3g–l). However, considerable roughness was observed on the surface of SPVA. The roughness of the SPVA surface could be due to functionalization of sulfonic acid groups on the surface of PVA. This observation supported successful synthesis of SPVA.

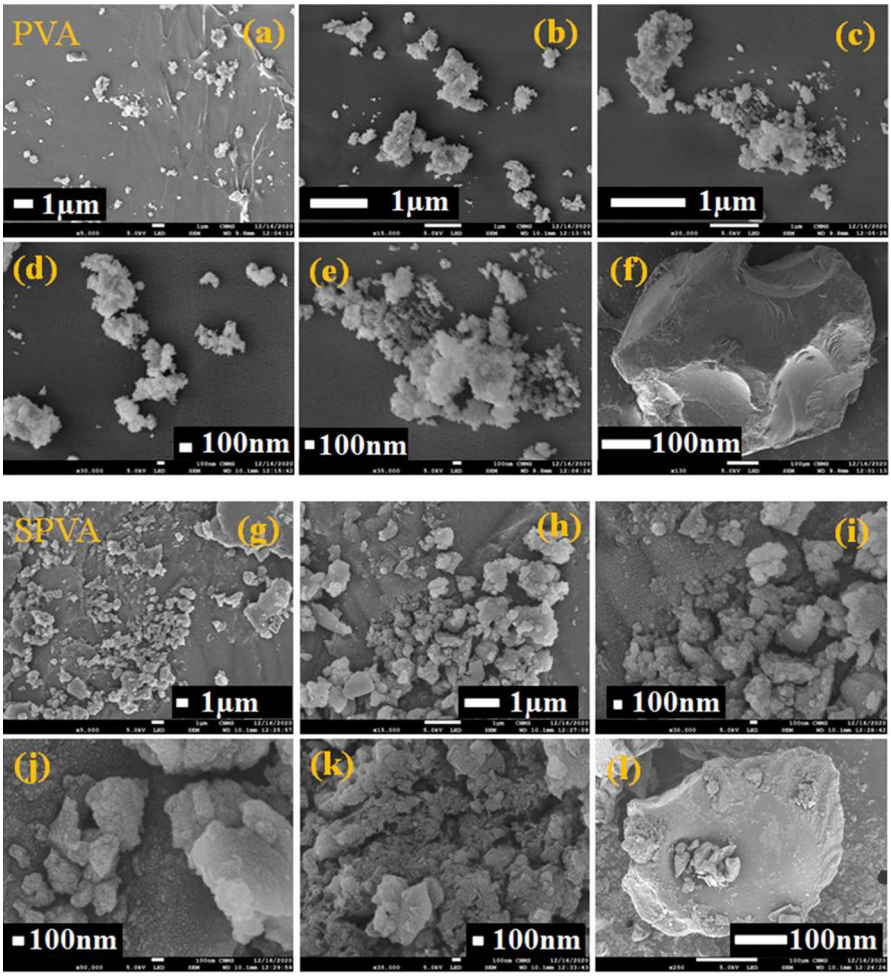


Fig. 3 FESEM analysis of **a–f** PVA and **g–l** SPVA

The elemental analysis of pristine PVA and SPVA was performed, and the results are displayed in Fig. 4a, b. Elemental analysis of pristine PVA confirmed that the PVA is comprised of only carbon and oxygen in stoichiometric amount (Fig. 4a). The presence of only C and O suggested that pristine PVA is highly pure with no impurities in it. Further, in elemental analysis of SPVA along with carbon and oxygen, sulfur was also detected (Fig. 4b). The presence of sulfur in stoichiometric amount confirmed the successful formation of SPVA. The mapping analysis of pristine PVA and SPVA was performed, and the results are displayed in Fig. 4c, d. Mapping analysis of pristine PVA confirmed the presence of expected elements in the PVA (Fig. 4c). Additionally, in mapping analysis SPVA sulfur was detected in sufficient amount along with C and O (Fig. 4d). The EDAX and mapping analysis therefore confirmed the successful formation of SPVA.

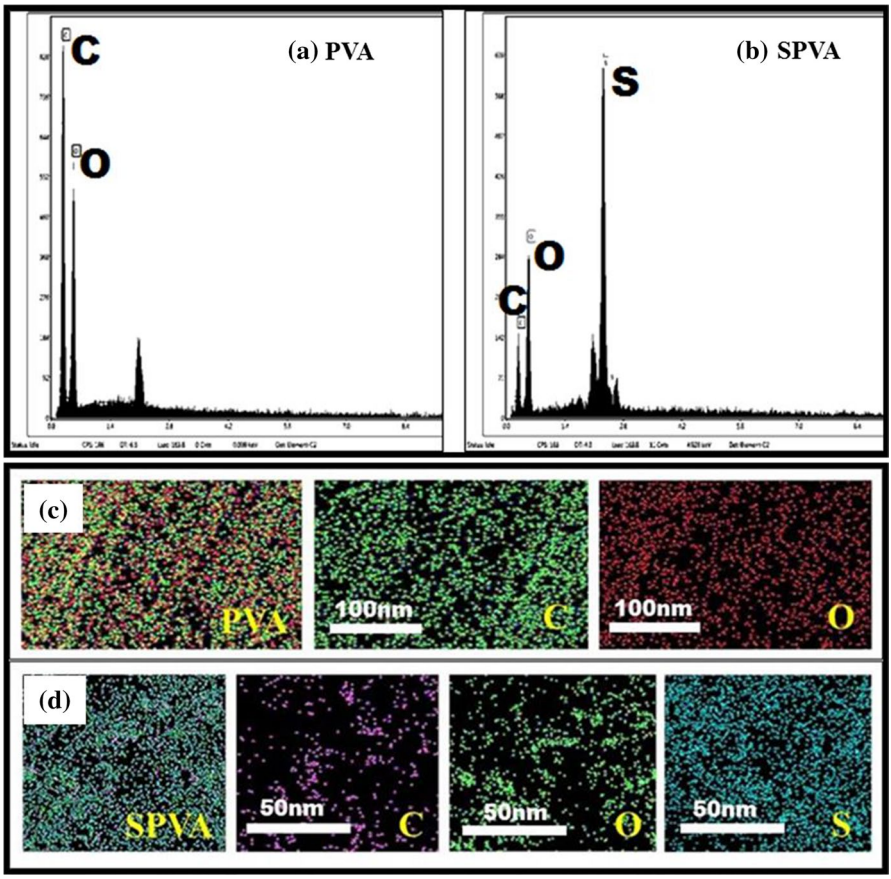


Fig. 4 Elemental analysis of **a** PVA and **b** SPVA and elemental mapping of **c** PVA and **d** SPVA

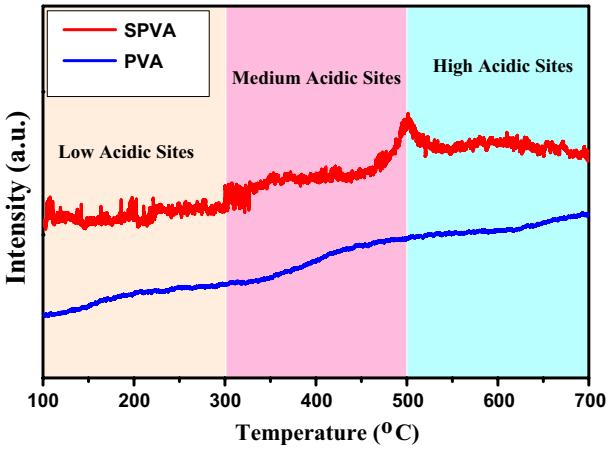


Fig. 5 NH_3-TPD profile of PVA and SPVA

NH_3-TPD analysis

The acidity of catalyst is a vital factor that governs the reactions involving synthesis of pyrazole. Therefore, NH_3-TPD analysis was performed to quantify the amount and the strength of acidic sites present in SPVA catalyst. NH_3-TPD graph of PVA and SPVA catalyst is presented in Fig. 5. In order to interpret the graph, it is important to understand the classification of different acidic regions with respect to the temperature range. The peaks arising in the temperature range 100–300 °C correspond to the weak acidic sites, moderate acidic sites appear in the 300–500 °C temperature range, and peaks related to the strong acidic sites appear above 500 °C. In NH_3-TPD plot of pristine PVA, no defined peak was observed in any of the three regions [38]. The observation suggested that PVA does not exhibit acidic character and the total acidity calculated from TPD data was 0.04 mmol/g. The NH_3-TPD analysis of SPVA was also performed which displayed a prominent peak in the temperature region > 500 °C. This suggested that functionalization of PVA with sulfonic acid group considerably generated strong acidic sites in SPVA catalyst [39]. The total acidity calculated for SPVA was 0.1 mmol/g. Hence, the successful incorporation of sulfonic acid groups in PVA was confirmed by NH_3-TPD analysis.

Table 1 Screening of reaction conditions for the SPVA-catalyzed synthesis of pyrazole

Entry	Catalyst	Catalyst amount (wt%)	Solvent	Temp (°C)	Time (h)	Conv. (%)	Selec. (%)	Yield (%)[a]
1	–	–	–	R.T	24	0	0	0
2	–	–	–	R.T	48	0	0	0
3	–	–	–	90	24	20	25	5
4	PVA	3	–	90	24	45	44	20
5	PVA	5	–	90	24	50	72	36
6	SPVA	5	–	R.T	12	60	58	35
7	SPVA	3	–	90	24	65	77	50
8	SPVA	5	–	90	03	100	89	89
9	SPVA	10	–	90	03	100	92	92
10	SPVA	15	–	90	03	100	94	94
11	SPVA	5	EtOH	90	05	100	68	68
12	SPVA	5	DCM	90	06	100	72	72
13	SPVA	5	Acetonitrile	90	05	100	80	80
14	SPVA	5	THF	90	04	100	78	78

All reactions proceed with equivalent mmol (1.0 mmol) of benzaldehyde, malononitrile and phenylhydrazine reactants

[a]Yield refers to isolated product which characterized by ^{1}H, ^{13}C NMR

Catalytic activity of SPVA toward synthesis of pyrazole derivatives

The characterization results confirmed the functionalization of sulfonic acid groups on the polyvinyl alcohol. Additionally, development of acidic sites in SPVA catalyst was also confirmed by NH_3-TPD analysis. This solid Bronsted acidic SPVA catalyst was then investigated for its activity toward synthesis of pyrazole by a one-pot multicomponent reaction of aromatic aldehyde with malononitrile and phenyl hydrazine. With regard to this, certain controlled experiments were performed to investigate the individual role of different parameters responsible for the formation of pyrazole. The result of these reactions is displayed in Table 1. To begin with, a neat reaction was performed in the absence of catalyst and solvent for 24 h by charging 1 mmol of each reactant at room temperature (R.T). However, no conversion and yield were observed toward the desired product (Table 1, Entry 1). The above reaction was continued and performed for 48 h with constant stirring at R.T. Still, there was no indication of pyrazole formation from TLC, which suggests that the presence of catalyst and/or co-catalyst is essential for driving the reaction in forward direction to obtain desired product (Table 1, Entry 2). Further, the reaction was conducted by increasing the reaction temperature to 90 °C under similar reaction condition in order to determine the effect of temperature on the reaction progress. The reaction resulted in 20% conversion with only 5% yield toward pyrazole (Table 1, Entry 3). The result demonstrated that it is difficult for the reaction to proceed only with the assistance of temperature as the energy is not sufficient for obtaining the product in high yields.

In order to determine the catalytic activity of PVA, a reaction was performed in the presence of 3 wt% PVA as a catalyst at 90 °C for 24 h reaction period. As anticipated, the conversion increased to 45% with low yield toward pyrazole (Table 1, Entry 4). Further, to study the effect of PVA loading on the activity, the amount of PVA catalyst was increased to 5 wt% and then the reaction was performed at 90 °C for 24 h. The reaction delivered a slight increase in conversion of around 50% and selective yield of 36% (Table 1, Entry 5). These results suggest that PVA as a catalyst is not efficient enough for the transformation of aromatic aldehyde, malononitrile and phenyl hydrazine into corresponding pyrazole derivative. To investigate the influence of SPVA catalyst toward the formation of pyrazole, the reaction was performed in the presence of 5 wt% of SPVA catalyst at R.T for 12 h. The reaction displayed 60% conversion and 35% yield toward pyrazole (Table 1, Entry 6). The result revealed that SPVA as a catalyst was able to drive the reaction in positive direction to some extent. However, yield toward pyrazole was low. Therefore, the effect of SPVA catalyst loading was studied at 90 °C by varying the catalyst loading by 3, 5, 10 and then 15 wt%. The 3 wt% SPVA-catalyzed reaction led to the conversion of 60% with 35% of product yield in 12 h of reaction time (Table 1, Entry 7). Low catalytic activity evidenced at low loading of SPVA catalyst can possibly be due to availability of less acidic sites for the reaction to take place [40]. Surprisingly, with 5 wt% SPVA catalyst the reaction resulted in 100% conversion with admirable yield of 89% in 3 h of reaction time (Table 1, Entry 8). The reason for the better catalytic activity could be due to effective collisions and thus interaction of reactants with the sufficient acidic sites of 5 wt% SPVA catalyst at 90 °C of reaction temperature

[40]. The presence of acidic sites in SPVA catalyst was evidenced by NH_3-TPD. These promising results demonstrated that SPVA as a catalyst can deliver better catalytic performance if appropriate temperature and catalyst amount are provided for the reaction. Further, with 10 and 15 wt% SPVA catalyst, the reaction resulted in complete conversion with a gradual increase in the pyrazole yield (92 and 94%), respectively (Table 1, Entries 9, 10). The effect of SPVA catalyst loading study suggested that with an increase in the amount of SPVA catalyst there was no noticeable increase in the yield toward the desired pyrazole product. Also, it is always desirable to achieve appreciable catalytic activity at low catalyst loading. Therefore, 5 wt% SPVA catalyst loading and 90 °C reaction temperature were chosen as the optimum reaction parameters that aided in achieving maximum of 89% yield toward corresponding pyrazole in solvent-free condition.

Even though the 5 wt% SPVA catalytic system proved highly efficient in solvent-free condition, we further studied the effect of different solvents on reaction. To begin with, when we conducted the reaction with ethanol as a solvent at optimized reaction conditions, we obtained 100% conversion (Table 1, Entry 11). Nevertheless, there was a decrease in the yield of product (Table 1, Entry 11). On performing the reaction in presence of DCM as a solvent under optimized reaction conditions, we observed a decrease in the yield of pyrazole even though there was steadiness in the conversion (Table 1, Entry 12). Subsequently, the solvent was replaced by acetonitrile and the reaction was performed under optimized reaction conditions. Substantial yield toward the desired pyrazole product was obtained with complete conversion (Table 1, Entry 13). Finally, THF as a solvent was employed in the reaction, which resulted in the product yield of 78% with 100% conversion within 4 h of reaction time (Table 1, Entry 14). These results revealed that in the presence of different solvents the reaction showed 100% conversion and, however, failed to cross the yield of pyrazole above 90%. Despite the fact that good to moderate yields toward the pyrazole product were obtained in acetonitrile and THF solvents, it is also better to perform the reaction in solvent-free condition to justify the green chemistry principles. Therefore, the reaction was preferred to be performed under optimized reaction conditions in the absence of the solvent.

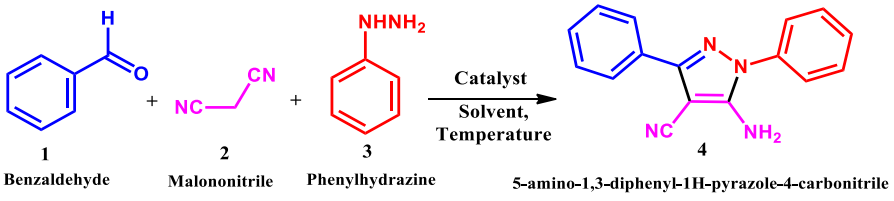


Table 2 Synthesis of pyrazole using different heterogeneous catalysts and their comparison with SPVA in optimized reaction condition

Entry	Catalyst	Catalyst dosage (wt%)	Time (h)	Conv. (%)	Yield (%)[a]
1	$ZnCl_2$	5	8	79	52
2	$NiCl_2$	5	9	90	60
3	$FeCl_3$	5	6	88	66
4	$AlCl_3$	5	7	86	58
5	$CuCl_2.2H_2O$	5	9	68	42
6	$SnCl_2$	5	7	80	54
7	BF_3	5	4	100	68
8	CH_3COOH	5	10	100	66
9	SPVA	5	3	100	89

All reactions proceed with equivalent mmol (1.0 mmol) of benzaldehyde, malononitrile and phenylhydrazine reactants and 5 wt% catalyst dosage

[a]Yield refers to isolated product characterized by ^{1}H NMR, ^{13}C NMR

Comparison of present catalytic system with known catalysts for pyrazole synthesis

To compare the efficient catalytic activity of SPVA catalyst with other known catalysts, we conducted the model reaction of pyrazole synthesis by using optimized reaction conditions in the presence of different catalysts and the obtained results are shown in Table 2. Several metal-based precursors were used for studying their catalytic effect on the synthesis of pyrazole. Precisely, pyrazole synthesis reaction was performed in the presence of $ZnCl_2$ catalyst under optimized reaction conditions. The reaction progressed slowly to yield 52% of desired product in time period of 8 h (Table 2, Entry 1). Further, the reaction was performed in the presence of $NiCl_2$ and $FeCl_3$ as a catalyst which presented respective yield of 60% and 66% toward pyrazole (Table 2, Entries 2, 3). Subsequently, we also employed $AlCl_3$ and $CuCl_2$ as a homogeneous catalyst for the synthesis of pyrazole. $AlCl_3$ demonstrated 58%, while $CuCl_2$ resulted in 42% yield toward pyrazole (Table 2, Entries 4, 5). In addition, $SnCl_2$ as a catalyst was able to produce average yield of the desired product even after proceeding reaction for 7 h (Table 2, Entry 6). Subsequently, we carried out the reaction with BF_3 which is a strong Lewis acid. The catalyst displayed 100% conversion within short period of time (Table 2, Entry 7). However, the catalyst was not efficient enough to deliver good yield toward the pyrazole product (Table 2, Entry 7). In another attempt, we tried to employ homogeneous CH_3COOH catalyst that could provide more acidic condition for the synthesis of pyrazole. The catalyst demonstrated complete conversion with 66% yield (Table 2, Entry 7). Remarkably, in comparison with the activity of all the above catalysts, SPVA catalyst seemed to deliver outstanding catalytic performance under optimized reaction conditions (Table 2, Entry 8). One major drawback of rest of the catalytic systems is that they are homogeneous in nature and their separation from reaction

Table 3 Synthesis of different substituted pyrazole derivatives using SPVA catalyst in optimized reaction condition

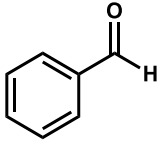
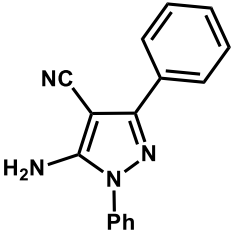
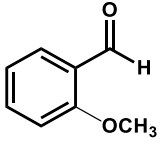
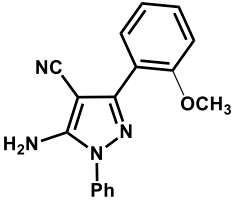
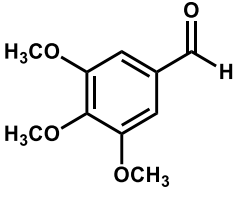
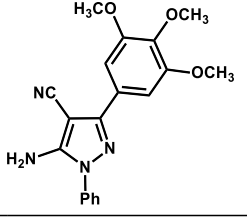
Entry	Aldehyde	Malononitrile	Phenyl hydrazine	Time (h)	Product	Yield (%)[a]	Melting point (°C)	
							Found	Literature
1			Ph–NH–NH_2	3		89	158–159	161 [41]
2			Ph–NH–NH_2	3		82	130–131	130–132 [41]
3			Ph–NH–NH_2	3.5		74	128–130	130–131 [41]

Table 3 (continued)

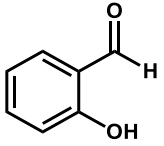
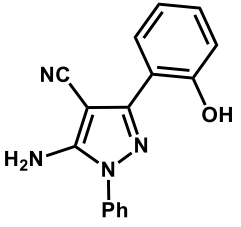
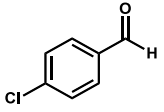
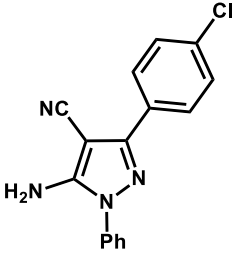
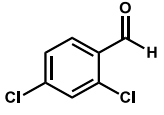
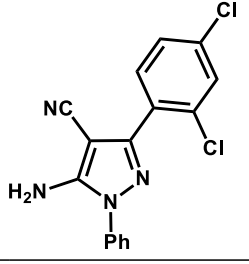
Entry	Aldehyde	Malononitrile	Phenyl hydrazine	Time (h)	Product	Yield (%)[a]	Melting point (°C)	
							Found	Literature
4			$Ph–NH–NH_2$	3		68	159	160–162 [41]
5			$Ph–NH–NH_2$	2.5		82	128–129	129 [41]
6			$Ph–NH–NH_2$	2		84	162–163	161–162 [41]

Table 3 (continued)

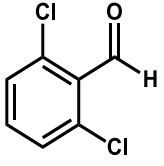
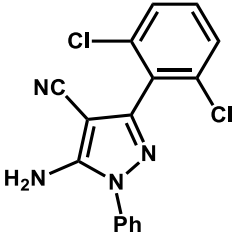
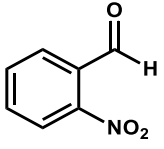
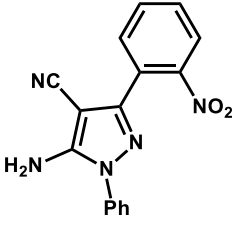
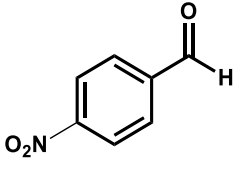
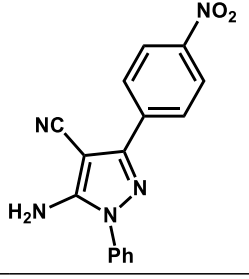
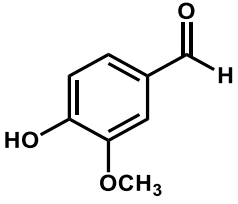
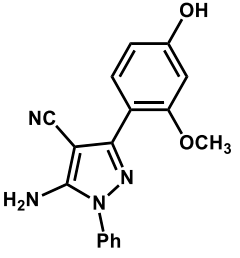
Entry	Aldehyde	Malononitrile	Phenyl hydrazine	Time (h)	Product	Yield (%)[a]	Melting point (°C)	
							Found	Literature
7			$Ph–NH–NH_2$	2		80	158–159	159–161 [41]
8			$Ph–NH–NH_2$	1.5		89	160–161	160–162 [41]
9			$Ph–NH–NH_2$	1.5		86	161–162	164–165 [19]

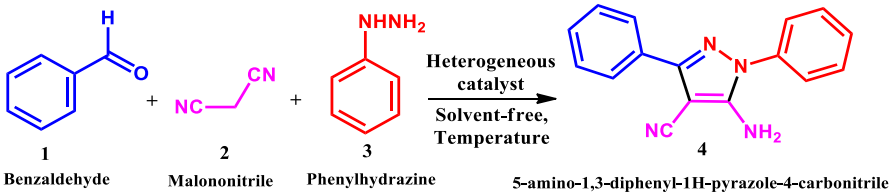
Table 3 (continued)

Entry	Aldehyde	Malononitrile	Phenyl hydrazine	Time (h)	Product	Yield (%)[a]	Melting point (°C)	
							Found	Literature
10			$Ph–NH–NH_2$	2.5		78	156–158	158–159 [41]

All reaction proceed with equivalent mmol (1.0 mmol) of reactant and 5 wt% SPVA catalyst

[a]Yield refers to isolated product which characterized by ^{1}H NMR, ^{13}C NMR

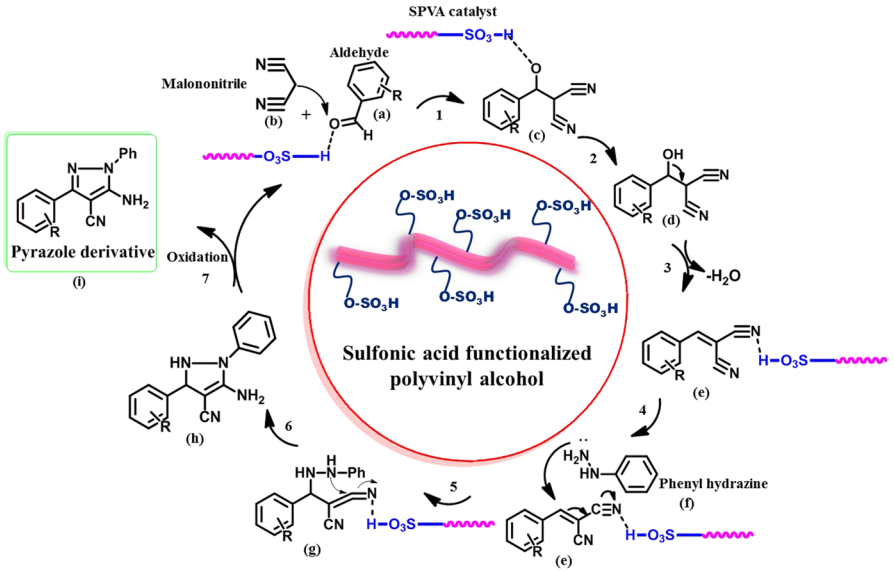
mixture is quite tedious. In contrary, the present SPVA catalytic system being heterogeneous in nature can be easily separated and recycled for several times.



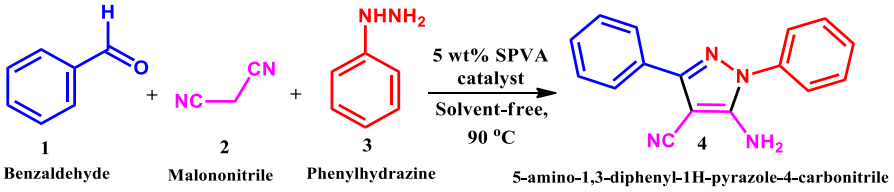
Synthesis of different pyrazole derivatives from substituted aromatic aldehydes by using SPVA catalyst

As evidenced from the above study, SPVA catalyst displayed remarkable catalytic activity for the synthesis of pyrazole in comparison with the rest of the investigated homogeneous catalysts. We further attempted to investigate the effect of SPVA catalyst for the synthesis of different pyrazole derivatives from substituted aromatic aldehyde. Consequently different commercially available substituted aromatic aldehyde, malononitrile and phenyl hydrazine were treated under the optimized reaction conditions for the synthesis of various pyrazole derivatives, and the results are summarized in Table 3.

All substituted aldehyde, malononitrile and phenyl hydrazine participated well in this cyclization to afford the desired product with efficient yield. The reaction was completed within short period of time in the presence of catalytic amount of SPVA. Initially, when treating benzaldehyde with the malononitrile and phenyl hydrazine under optimized reaction conditions, the reaction showed 89% selective yield of corresponding pyrazole in 3 h (Table 3, Entry 1). When the reaction was carried out with aldehydes consisting of electron-donating group such methoxy, trimethoxy and hydroxyl groups, 82%, 74% and 68% of pyrazole derivative yield were obtained, respectively (Table 3, Entries 2–4). Further, chlorine (electron-withdrawing group)-substituted benzaldehydes demonstrated excellent yield of corresponding pyrazole derivatives as compared to the electron-releasing groups (Table 3, Entries 5–7). Interestingly, reaction consisting of aromatic aldehyde substituted $–NO_2$ as an electron-withdrawing group presented 100% conversion with 89% and 86% yield, respectively (Table 3, Entries 8, 9). Finally, the reaction was carried out with vanillin, malononitrile and phenyl hydrazine with 5wt% of SPVA catalyst loading which yielded 78% of corresponding pyrazole derivative (Table 3, Entry 10). From the above discussion, we may conclude that SPVA can be considered as a highly suitable and competent catalyst for the synthesis of pyrazole derivatives with various functional substitutions on aromatic ring.



Scheme 1 Plausible mechanism for synthesis of pyrazole derivatives by using aldehyde, malononitrile and phenyl hydrazine in the presence of SPVA catalyst



Proposed plausible mechanism for SPVA-catalyzed three-component reaction for synthesis of pyrazole

SPVA catalyst with acidic sites initiated the mechanism for formation of 5-amino-1*H*-pyrazole-4-carbonitrile, which is presented in Scheme 1. The reaction commenced when SPVA catalyst activated carbonyl group of aldehyde (a) and malononitrile (b) to form intermediate (c) (Step 1). The SPVA catalyst serves as a proton donor for intermediate (c) to form intermediate (d) (Step 2). Further, intermediate (e) was obtained by elimination of water molecule (Step 3). Intermediate (e) was then attacked by phenyl hydrazine (f) by Michael addition to form the final product 5-amino-1*H*-pyrazole-4-carbonitrile via intermediate (g) and (h) (Steps 4–7). Precisely, the electron deficiency was generated in malononitrile due to withdrawal of lone pair of electron on nitrogen by SPVA catalyst (Steps 4, 5). This deficiency of

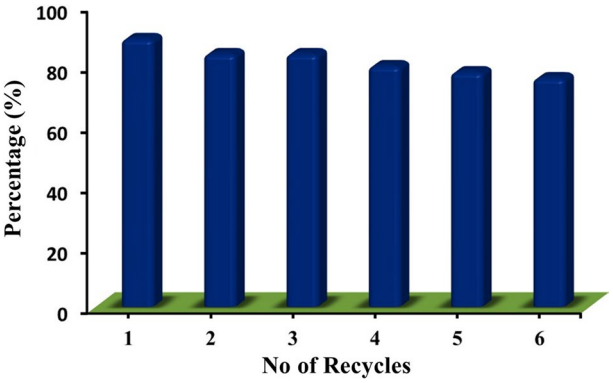


Fig. 6 Recyclability study of SPVA catalyst for pyrazole synthesis

electrons on nitrogen of malononitrile assisted the reaction to proceed with faster rate which further aided the cyclization process (Step 6). Finally, the corresponding product underwent oxidation to yield the desired product 5-amino-1*H*-pyrazole-4-carbonitrile (Step 7). The mechanism is well supported by the literature [42].

Recyclability studies

The recyclability study of heterogeneous catalysts is of extreme importance in industrial viewpoint [43–45]. Therefore, we performed recyclability study of SPVA catalyst by simply filtering the catalyst from the reaction mixture, washing it several times with distilled water and finally drying under vacuum in a microwave oven. The dried SPVA catalyst was then employed in the stoichiometric amount for the same reaction. In this way, the recyclability of the catalyst was studied up to several cycles. The results in Fig. 6 showed that the SPVA catalyst displayed consistency in the catalytic activity for the synthesis of pyrazole derivative up to six recycles. Additionally, the FESEM analysis was performed of the reused SPVA catalyst after sixth catalyst which showed no change in the morphology of the reused catalyst, which suggests that the catalyst can efficiently be employed for the scale-up reactions. Therefore, the present methodology illustrates green approach and environmental friendly synthesis for pyrazole derivative under solvent-free condition.

Conclusion

In conclusion, we report the synthesis of an efficient acidic SPVA as a heterogeneous catalyst by a simple, one-step functionalization of PVA with sulfonic acid groups. The successful formation of SPVA catalyst was confirmed, and its physiochemical properties were revealed by making use of several advanced characterization techniques. After confirmation of its successful formation, the SPVA catalyst was then explored for its activity toward the synthesis of pyrazole derivatives. The acidic SPVA catalyst demonstrated complete conversion with appreciable yield of

89% toward pyrazole in 3-h reaction time. We have also put in efforts to investigate and propose a plausible mechanism for the SPVA-catalyzed pyrazole synthesis reaction. Recyclability study of SPVA catalyst also demonstrated that it can effectively be separated and recycled up to six recycles without appreciable loss in its catalytic activity. To conclude, the present synthetic protocol for three-component synthesis of pyrazole derivatives in the presence of SPVA as a heterogeneous catalyst can be considered as a sustainable approach as the process justified the overarching goals of green chemistry.

Acknowledgements This work was supported by Centre for Nano and Material Sciences (CNMS), JAIN (Deemed-to-be University), Bangalore, and funding support was through the basic research Grant of JAIN (No. 11(39)/17/005/2017SG). Authors would like to thank Nano Mission, DST, Government of India, for partial financial support SR/NM/NS-20/2014.

Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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