Research Article

Knoevenagel Condensation of Aldehydes with Ethyl Cyanoacetate in Water Catalyzed by P4VP/ Al_2O_3 - SiO_2

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Received 28 June 2012; Revised 9 September 2012; Accepted 25 September 2012

Academic Editor: Radhey Srivastava

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This paper reports the preparation and characterization of poly(4-vinylpyridine) (P4VP) supported on Al_2O_3 - SiO_2 and its application for Knoevenagel condensation reaction of various aldehydes with ethyl cyanoacetate in water as a green solvent. The results illustrate that the sample containing 0.6 molar ratio of Al to Si exhibits the highest yield (98%) in the reaction of benzaldehyde with ethyl cyanoacetate with 100% selectivity to the arylidene derivative.

1. Introduction

The development of heterogeneous catalysts for special chemical synthesis has become a major area of research. The potential advantage of these materials (simplified recovery and reusability) over homogeneous systems can lead to environmentally benign chemical procedures in academia and industries. The application of solid acidic and basic catalysts in clean technologies and sustainable chemistry is a green alternative for chemical processes. The materials provide high yield and selectivity along with waste reduction, easier catalyst recovery procedures, and safer and easier operation methods.

Recently, many attempts have been made to develop polymer-supported catalysts on inorganic surfaces. It provides convenience of workup and product purification, lower environmental hazards, and in most cases, reusability of the polymer-supported catalysts. These materials combine some advantages of organic compounds (easy processing with conventional techniques, elasticity, and organic functionalities) with properties of inorganic oxides (hardness, thermal and chemical stability, and transparency). Therefore, they have attracted considerable attention [1, 2]. Moreover, the use of these materials offers a striking and practical method for clean and efficient preparation of novel chemical libraries

with potential application in the pharmaceutical or agrochemical industries.

The Knoevenagel condensation reaction is one of the most important C-C bond-forming reactions in organic chemistry. In general, this type of condensation reaction performs in homogeneous solution in the presence of organic bases [3]. This method has its limitations such as difficulties in catalyst separation and recycling. In order to reduce effluents to environmentally acceptable limits, this transformation has been studied by using various heterogeneous solid bases [4], for instance, hydrotalcite [5], hydroxyapatite-encapsulated γ - Fe_2O_3 [6], MCM-41 [7], modified silica gel [8], MgO/ZrO_2 [9], and guanidine [10].

In the present study, to develop heterogeneous basic catalysts on mesoporous material [11, 12], here, we report the synthesis and characterization of poly(4-vinylpyridine)/ Al_2O_3 - SiO_2 (P4VP/ Al_2O_3 - SiO_2) as a nano-pore catalyst by in situ polymerization of 4-vinylpyridine in the presence of Si and Al precursors. The catalytic performance of the nano composite was investigated for the Knoevenagel condensation of some aromatic and aliphatic aldehydes with active methylene reagents. In addition, catalytic activity of the composites prepared through two methods (in situ and impregnated methods) was investigated, and also a comparison was made between the basic catalytic properties

of P4VP/ Al_2O_3 - SiO_2 , P4VP/ Al_2O_3 , and P4VP/ SiO_2 composites.

2. Experimental

2.1. Techniques. The obtained materials were characterized by X-ray diffraction (Bruker D8ADVANCE, Cu $K\alpha$ radiation), FT-IR spectroscopy (Nicolet 400D in KBr matrix in the range of 4000–400 cm^{-1}), BET specific surface areas and BJH pore size distribution (Series BEL SORP 18, at 77 K), scanning electron microscopy using PhilipsXL30 with SE detector, and back titration using NaOH (0.1 N).

2.2. Catalyst Preparation

2.2.1. Synthesis of P4VP/ Al_2O_3 - SiO_2 by In Situ Method. Aluminum isopropoxide (98%) (2 mL, 10 mmol) was dissolved in *n*-butanol (60 mL) in a round-bottom flask equipped with magnetic stirrer and a condenser. The mixture was heated to 80°C. Then, to the clear solution, acetyl acetone (H-acac, 2.064 mL, 0.02 mol) and tetraethyl orthosilicate (98%) (2 mL, 10 mmol) were added sequentially and rapidly. Following the addition, a transparent solution was observed after 5 minutes of stirring. Then, 4-vinylpyridine (2 mL, 18.5 mmol) and potassium peroxodisulfate (0.5 g, 1.85 mmol) were added to the reaction mixture under continuous stirring at 80°C. After 1 h, the solution was cooled down to room temperature, and deionized water (10 mL) was added slowly as the hydrolyzing agent. The solution was left for 48 hours at room temperature to hydrolyze the alkoxides, yielding a transparent gel. It was dried at 60°C, and white fine solid powder was obtained. By varying the Al/Si molar ratio from 1.66 to 0.6, various P4VPs/ Al_2O_3 - SiO_2 were also prepared for comparative purposes. The samples were named P4VP/ Al_2O_3 - $\text{SiO}_2(x)$ (in situ) (where x = Al/Si molar ratio which varies from 1.66 to 0.6).

The amount of basic sites of the polymer-supported samples was estimated by back titration using NaOH (0.1 N). The distinct amount of the catalyst was stirred in HCl (0.5 N) for 30 minutes. Then, the mixture was filtrated and titrated with NaOH (0.1 N). The amounts of basic sites of P4VP/ Al_2O_3 - $\text{SiO}_2(1.66)$ (in situ), P4VP/ Al_2O_3 - $\text{SiO}_2(1)$ (in situ), and P4VP/ Al_2O_3 - $\text{SiO}_2(0.6)$ (in situ) were found to be 4.95, 5.15, and 5.86 mmol g^{-1} , respectively.

2.2.2. Synthesis of P4VP/ SiO_2 by In Situ Method. Tetraethyl orthosilicate (98%) (2 mL, 9 mmol) and ethanol (2.3 mL, 45 mmol) were stirred at room temperature. Then, the mixture of 2 mL of 4-vinylpyridine, potassium peroxodisulfate (0.5 g, 1.85 mmol), and 1.05 mL of aqueous nitric acid (0.05 mL HNO_3 and 1 mL H_2O) slowly added was stirred at room temperature for 30 minutes. The solution was heated to 80°C, and the components were thoroughly mixed. After 2 hours, the reaction mixture was cooled down to room temperature, and ethanol (5.11 mL, 100 mmol) was added slowly. The resulting solid product was filtered and washed with deionized water and then dried at 60°C. The sample

was named as P4VP/ SiO_2 , and the amount of basic sites was 2.26 mmol g^{-1} .

2.2.3. Synthesis of P4VP/ Al_2O_3 by In Situ Method. For the preparation of another base catalyst, the relevant aluminum isopropoxide (98%) was used to reach the same molar ratio as it was done for P4VP/ SiO_2 . The obtained sample was termed as P4VP/ Al_2O_3 , and the amount of basic sites was 2.75 mmol g^{-1} .

2.2.4. Synthesis of P4VP/ Al_2O_3 - SiO_2 by Impregnated Method. Al_2O_3 - SiO_2 was used as the support, which was prepared by the optimized Al/Si molar ratio, described in the previous work [12, 13]. A mixture of 4-vinylpyridine (2 mL, 18.5 mmol) and benzoyl peroxide (0.134 g, 0.556 mmol) in 15 mL of tetrahydrofuran (THF) was refluxed by stirring it for 4 hours. In this step, poly(4-vinylpyridine) was produced. Then, Al_2O_3 - $\text{SiO}_2(0.6)$ (1.6 g) was added to the reaction mixture, and it was refluxed for another 2 hours. On completion, the solvent was removed by vacuum filtration and, the residue was washed by tetrahydrofuran (3×10 mL) and dried at 60°C under reduced pressure. The sample was termed as P4VP/ Al_2O_3 - $\text{SiO}_2(0.6)$ (imp), and the amount of basic sites was 1.32 mmol g^{-1} .

2.3. General Procedure for the Knoevenagel Condensation. In a typical experiment, 2 mmol of benzaldehyde (0.20 mL), 2 mmol of ethyl cyanoacetate (0.21 mL), and 0.04 g of catalyst (P4VP/ Al_2O_3 - SiO_2) taken in a round-bottom flask were refluxed under continuous stirring in H_2O as a solvent. The progress and completion of the reaction was monitored by TLC, using *n*-hexane/ethyl acetate (5:1) as an eluent. 30 minutes after the reaction, the mixture was cooled to 10°C for the purpose of solidification of the product, water was also removed by Buchner filtration. Afterwards, the residual solid was recrystallized by hot ethanol (5 mL), and the product was identified by ^1H -NMR, ^{13}C -NMR, and FT-IR spectroscopic techniques. The spectral data of some desired products are given as follows.

2-Propenoic Acid-2-Cyano-3-Phenyl Ethyl Ester (Table 7, Entry 1). White crystal solid, mp 49–51°C; (KBr, cm^{-1}): 1446, 1606 (C=C, aromatic), 1733 (C=O), 2221 (CN), 2982 (CH, str), 3029 (=CH, str), 3069 (CH, str, aromatic); ^1H -NMR (500 MHz, CDCl_3) δ 1.43 (CH_3 , t, 3H, J = 7.1 Hz), 4.42 (CH_2 , q, 2H, J = 7.1 Hz), 7.52–7.60 (ArH, m, 3H), 8.02 (ArH, d, 2H, J = 7.4 Hz), 8.28 (=CH, s, 1H); ^{13}C -NMR (125 MHz, CDCl_3) δ 14.59 (CH_3), 63.15 (O- CH_2), 103.49 (C-CN), 115.90 (CN), 129.71, 131.49, 131.92, 133.72, 155.44, 162.89 (C=O).

2-Propenoic Acid-2-Cyano-3-(3-Methyl Phenyl) Ethyl Ester (Table 7, Entry 3). White crystal solid, mp 82–85°C; IR (KBr, cm^{-1}): 1450, 1609 (C=C, aromatic), 1728 (C=O), 2218 (CN), 2908, 2982 (CH, str), 3022 (=CH, str); ^1H -NMR (500 MHz, CDCl_3) δ 1.44 (CH_3 , t, 3H, J = 7.1 Hz), 2.45 (CH_3 , s, 3H), 4.42 (CH_2 , q, 2H, J = 7.1 Hz), 7.39–7.44 (ArH, m, 2H), 7.81 (ArH, s, 1H), 7.85 (ArH, d, 1H, J = 7.3 Hz), 8.25 (=CH,

s, 1H); ^{13}C -NMR (125 MHz, CDCl_3) δ 14.59 (CH_3), 21.71 (CH_3 , aromatic), 63.11 ($\text{O}-\text{CH}_2$), 103.12 ($\text{C}-\text{CN}$), 115.97 (CN), 128.66, 129.59, 131.91, 132.12, 134.64, 139.56, 155.70, 163.04 ($\text{C}=\text{O}$).

2-Propenoic Acid-2-Cyano-3-(4-Methoxy Phenyl) Ethyl Ester (Table 7, Entry 5). White crystal solid, mp 81–82°C; IR (KBr, cm^{-1}): 1435, 1510, 1585 ($\text{C}=\text{C}$, aromatic), 1722 ($\text{C}=\text{O}$), 2213 (CN), 2841, 2990 (CH , str.), 3021 ($=\text{CH}$, str.); ^1H -NMR (500 MHz, CDCl_3) δ 1.43 (CH_3 , t, 3H, $J = 7.1$ Hz), 3.93 (CH_3O , s, 3H), 4.40 (CH_2 , q, 2H, $J = 7.1$ Hz), 7.03 (ArH, d, 2H, $J = 8.9$ Hz), 8.04 (ArH, d, 2H, $J = 8.9$ Hz), 8.21 ($=\text{CH}$, s, 1H); ^{13}C -NMR (125 MHz, CDCl_3) δ 14.63 (CH_3), 56.05 (CH_3O), 62.86 ($\text{O}-\text{CH}_2$), 99.84 ($\text{C}-\text{CN}$), 116.65 (CN), 115.20, 124.82, 134.07, 154.82, 164.22, 163.56 ($\text{C}=\text{O}$).

2-Propenoic Acid-3-(2-Chloro Phenyl)-2-Cyano Ethyl Ester (Table 7, Entry 6). White crystal solid, mp 52–54°C; IR (KBr, cm^{-1}): 1470, 1603 ($\text{C}=\text{C}$, aromatic), 1728 ($\text{C}=\text{O}$), 2224 (CN), 2919 (CH , str.), 2992 ($=\text{CH}$, str.), 3064 (CH , str, aromatic); ^1H -NMR (500 MHz, CDCl_3) δ 1.44 (CH_3 , t, 3H, $J = 7.2$ Hz), 4.44 (CH_2 , q, 2H, $J = 7.2$ Hz), 7.43–7.55 (ArH, m, 3H), 8.27 (ArH, d, 1H, $J = 7.6$ Hz), 8.72 ($=\text{CH}$, s, 1H); ^{13}C -NMR (125 MHz, CDCl_3) δ 14.56 (CH_3), 63.38 ($\text{O}-\text{CH}_2$), 106.64 ($\text{C}-\text{CN}$), 115.24 (CN), 127.89, 130.31, 130.77, 134.09, 136.87, 151.59, 162.24 ($\text{C}=\text{O}$).

2-Propenoic Acid-2-Cyano-3-(4-Nitro Phenyl) Ethyl Ester (Table 7, Entry 7). Yellow crystal solid, mp 165°C; IR (KBr, cm^{-1}): 1516 ($\text{C}=\text{C}$, aromatic), 1722 ($\text{C}=\text{O}$), 2219 (CN), 2990 (CH , str.), 3096 ($=\text{CH}$, str.); ^1H -NMR (500 MHz, CDCl_3) δ 1.46 (CH_3 , t, 3H, $J = 7.2$ Hz), 4.46 (CH_2 , q, 2H, $J = 7.2$ Hz), 8.17 (ArH, d, 2H, $J = 8.8$ Hz), 8.34 ($=\text{CH}$, s, 1H), 8.39 (ArH, d, 2H, $J = 8.8$ Hz).

2-Propenoic Acid-2-Cyano-3-(2-Furanyl) Ethyl Ester (Table 7, Entry 8). White crystal solid, mp 85–87°C; IR (KBr, cm^{-1}): 1460, 1622 ($\text{C}=\text{C}$, aromatic), 1722 ($\text{C}=\text{O}$), 2219 (CN), 2990 (CH , str.), 3034 ($=\text{CH}$, str.), 3133 (CH , str, aromatic); ^1H -NMR (500 MHz, CDCl_3) δ 1.40 (CH_3 , t, 3H, $J = 7.2$ Hz), 4.38 (CH_2 , q, 2H, $J = 7.1$ Hz), 6.68 (ArH, q, 1H, $J = 1.2$ Hz), 7.41 (ArH, d, 1H, $J = 3.6$ Hz), 7.77 (ArH, d, 1H, $J = 1.5$ Hz), 8.03 ($=\text{CH}$, s, 1H); ^{13}C -NMR (125 MHz, CDCl_3) δ 14.58 (CH_3), 62.99 ($\text{O}-\text{CH}_2$), 99.08 ($\text{C}-\text{CN}$), 122.14 (CN), 114.28, 115.75, 139.88, 148.69, 149.17, 163 ($\text{C}=\text{O}$).

2-Propenoic Acid-2-Cyano-3-Pentyl Ethyl Ester (Table 7, Entry 9). Colorless oil; ^1H -NMR (500 MHz, CDCl_3) δ 7.78 (t, $J = 7.8$ Hz, H-olefinic), 4.55 (q, $J = 6.5$ Hz, 2H, OCH_2CH_3), 2.68 (q, $J = 7.7$ Hz, 2H, H-2), 1.5 (m, 2H, H-3), 1.6–1.4 (m, H-4,5 and OCH_2CH_3), 1.0 (CH_3 , m, 3H).

2-Propenoic Acid-2-Cyano-3-Cyclohexyl Ethyl Ester (Table 7, Entry 10). Colorless oil; ^1H -NMR (500 MHz, CDCl_3) δ 7.48 (d, $J = 9.7$ Hz, 1H, H-olefinic), 4.5 (q, $J = 7.2$ Hz, 2H, OCH_2CH_3), 2.9 (CH, m, 1H), 1.9 (CH_2 , m, 4H), 1.33 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 1.3–1.5 (CH_2 , m, 6H).

FIGURE 1: Powder XRD patterns of (a) Al_2O_3 - $\text{SiO}_2(0.6)$ and (b) $\text{P4VP}/\text{Al}_2\text{O}_3$ - $\text{SiO}_2(0.6)$ (in situ).

3. Results and Discussion

3.1. Characterization of the Catalyst. XRD patterns of Al_2O_3 - $\text{SiO}_2(0.6)$ and $\text{P4VP}/\text{Al}_2\text{O}_3$ - $\text{SiO}_2(0.6)$ (in situ) samples are shown in Figures 1(a) and 1(b). It can be seen that the spectrum of Al_2O_3 - $\text{SiO}_2(0.6)$ shows an amorphous form. The dispersive peak at $2\theta \approx 24^\circ$ is characteristic of noncrystalline SiO_2 , which is observed in both patterns (Figures 1(a) and 1(b)). After in situ polymerization of Al_2O_3 and SiO_2 by 4-vinylpyridine, the peaks at $2\theta \approx 17^\circ$ and 28° corresponding to the crystalline mullite phase are observed [14].

The FT-IR spectra of optimized polymer-supported samples are shown in Figure 2. The characteristic band at 1080–1100 cm^{-1} is due to the Si–O and Al–O stretching vibrations, which is seen in all samples. The absorption band for H–O–H bending vibration in water is around 1620–1650 cm^{-1} and 950 cm^{-1} . The spectra showed a broad band around 3100–3600 cm^{-1} , which is due to adsorbed water molecules. In the FT-IR spectra of composites (Figures 2(b), 2(d), and 2(f)), the new bands between 1410 and 1650 cm^{-1} are the characteristic absorptions of pyridine ring. Among them, the band appeared around 1600 cm^{-1} is attributed to the stretching vibration absorption of C–N bond, and the others are attributed to the stretching vibration absorption of C=C bond. In addition, the presence of peaks around 2900–3050 cm^{-1} corresponds to the aromatic and aliphatic C–H stretching, and the vibration at 856 cm^{-1} is for C–H deformation out of plane.

N_2 adsorption-desorption is a common method to characterize mesoporous materials. This method provides information about the specific surface area, average pore diameter and pore volume, and so forth. The nitrogen adsorption-desorption isotherm and structure data of the synthesized materials are presented in Figure 3 and Table 1, respectively.

TABLE 1: BET surface area and pore size analysis of the samples.

Catalyst	BET surface area (m ² /g)	Pore volume (cm ³ /g)	Average pore diameter (nm)	C constant	S _{BJH} (m ² /g)
Al ₂ O ₃ -SiO ₂ (0.6)	45.5	0.17	15.48	137.93	36.29
P4VP/Al ₂ O ₃ -SiO ₂ (0.6) (in-situ)	20.8	0.20	39.04	103.15	14.80

FIGURE 2: FT-IR spectra of (a) Al₂O₃, (b) P4VP/Al₂O₃, (c) SiO₂, (d) P4VP/SiO₂, (e) Al₂O₃-SiO₂(0.6), and (f) P4VP/Al₂O₃-SiO₂(0.6) (in situ).

Polymerization of 4-vinylpyridine in the Al₂O₃-SiO₂ structure led to a reduction in the specific surface area, which is probably due to the presence of poly(4-vinylpyridine) on the surface of catalyst. On the other hand, the data for the P4VP/Al₂O₃-SiO₂(0.6) (in situ) sample indicated a growth in the pore volume and pore diameter in comparison to Al₂O₃-SiO₂. The results are likely attributed to the presence of poly(4-vinylpyridine) in the structure of catalyst. Moreover, the amount of surface OH of the Al₂O₃-SiO₂ was eliminated upon polymerization which is why the C constant value of the BET equation decreased from 137.93 to 103.15 for Al₂O₃-SiO₂ and P4VP/Al₂O₃-SiO₂, respectively. Similarly, the surface area determined by BJH theory using the cumulative area of the pores also showed a significant drop (S_{BJH} (m²/g): 36.29 and 14.80 for Al₂O₃-SiO₂ and P4VP/Al₂O₃-SiO₂, resp.). According to the structure data of materials, it

FIGURE 3: Nitrogen adsorption-desorption isotherm at 77 K: (a) Al₂O₃-SiO₂(0.6) and (b) P4VP/Al₂O₃-SiO₂(0.6) (in situ).

can be said that the synthesized catalyst has nanosize pores, which is a suitable candidate for nanocatalyst for chemical purposes.

The SEM images of the polymer-supported Al₂O₃-SiO₂ are shown in Figures 4(a) and 4(b). These figures show the external surface morphology of the Al₂O₃-SiO₂ before (Figure 4(a)) and after the polymerization of 4-vinylpyridine (Figure 4(b)). It can be seen that the poly(4-vinylpyridine) particles distribute on the Al₂O₃-SiO₂ surface.

3.2. Catalytic Activity. The Knoevenagel condensation of benzaldehyde with ethyl cyanoacetate was chosen as a model reaction to test the catalytic activity of the poly(4-vinylpyridine)/Al₂O₃-SiO₂. Thus, the effect of various reaction parameters on the condensation of benzaldehyde with ethyl cyanoacetate was studied using P4VP/Al₂O₃-SiO₂ as a catalyst.

The variation of catalytic activity with changes in the Al/Si molar ratio of catalyst was studied, and the results are given in Table 2. It can be noted that the catalytic activity increases as the Al/Si molar ratio decreases. Moreover, the catalytic activity of poly(4-vinylpyridine)/Al₂O₃-SiO₂ prepared by in situ and impregnated methods was compared.

FIGURE 4: SEM images of (a) $\text{Al}_2\text{O}_3\text{-SiO}_2(0.6)$ and (b) $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (in situ).

TABLE 2: Effect of the Al/Si molar ratio on the catalytic activity of $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ ^a.

Catalyst	Yield ^b (%)
$\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(1.66)$ (in-situ)	91
$\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(1)$ (in-situ)	93
$\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (in-situ)	98
$\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (imp)	48

^a Reaction conditions: catalyst (0.12 g), benzaldehyde (2 mmol), ethyl cyanoacetate (2 mmol), reflux, H_2O (10 mL), reaction time = 30 min, selectivity = 100%. ^b Isolated yield.

TABLE 3: Effect of active methylene reagents on the Knoevenagel condensation over $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ (in-situ)^a.

Active methylene reagent	Time (min)	Yield ^b (%)
Ethyl cyanoacetate	30	98
Diethyl malonate	360	—
Acetoacetic ester	30	28

^a Reaction conditions: catalyst ($\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (in-situ), 0.12 g), benzaldehyde (2 mmol), active methylene reagent (2 mmol), reflux, H_2O (10 mL), and selectivity = 100%. ^b Isolated yield.

Polymer-supported surface acts as the proton scavenger to generate ethyl cyanoacetate anion, which acts as the attacking reagent. It attacks the carbonyl group of benzaldehyde and in subsequent steps produces arylidene derivative. When in situ method was used for the preparation of the catalyst, the polymerization of 4-vinylpyridine (4VP) was done in the presence of aluminium isopropoxide and tetraethyl orthosilicate. Therefore, the poly(4-vinylpyridine) has been dispersed properly in the structure of $\text{Al}_2\text{O}_3\text{-SiO}_2$ compared to impregnated method. Moreover, the results of back titration show that the amount of basic sites of $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ prepared by in situ method is more than $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ prepared by impregnated method. Hence, the organic polymer surface is more evenly distributed on the support surface in the case of the in situ method than impregnated method. Therefore, the former is more efficient as a basic catalyst than the latter

TABLE 4: Effect of solvent on the Knoevenagel condensation over $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ (in-situ)^a.

Solvent	Yield ^b (%)
Water	98
Methanol	47
Ethanol	55
Dichloromethane	0
Chloroform	0
Acetonitrile	0
Cyclohexane	0
Toluene	0
Solvent-free ^c	95

^a Reaction conditions: catalyst ($\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (in-situ), 0.12 g), benzaldehyde (2 mmol), ethyl cyanoacetate (2 mmol), reflux, solvent (10 mL), reaction time = 30 min, and selectivity = 100%. ^b Isolated yield. ^c Reaction temperature = 80°C. time = 50 min.

TABLE 5: Effect of reaction temperature on the Knoevenagel condensation over $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ (in-situ)^a.

Temperature (°C)	Time (min)	Yield ^b (%)
Room temperature	75	63
40	60	70
95	30	98

^a Reaction conditions: catalyst ($\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2(0.6)$ (in-situ), 0.12 g), benzaldehyde (2 mmol), ethyl cyanoacetate (2 mmol), H_2O (10 mL), and selectivity = 100%. ^b Isolated yield.

and leads to a higher yield of Knoevenagel condensation of benzaldehyde by ethyl cyanoacetate.

The activity of $\text{P4VP/Al}_2\text{O}_3\text{-SiO}_2$ for Knoevenagel condensation reaction was determined by using ethyl cyanoacetate, diethyl malonate, and acetoacetic ester as active methylene reagents (Table 3). It may be observed that the substrates have acidic methylene groups with pK_a near 9 and 11 (ethyl cyanoacetate and acetoacetic ester, resp.) and it can be deprotonated by the catalyst to generate the corresponding carbanion, followed by attacking an electron acceptor center.

TABLE 6: Effect of various supports on the Knoevenagel condensation^a.

Catalyst	Time (min)	Yield ^b (%)
Al ₂ O ₃ -SiO ₂ (0.6)	30	8
P4VP/Al ₂ O ₃ -SiO ₂ (0.6) (in-situ)	30	98
P4VP/Al ₂ O ₃	120	87
P4VP/SiO ₂	10	55

^a Reaction conditions: catalyst (0.04 g), benzaldehyde (2 mmol), ethyl cyanoacetate (2 mmol), reflux, H₂O (10 mL), and selectivity = 100%. ^b Isolated yield.

Moreover, it has been found that the catalyst is not able to pull off protons from diethyl malonate ($pK_a \approx 13$) and the Knoevenagel reaction with this substrate was not obtained. This observation is a further support that the catalyst has surface basic sites with pK_a lower than 13 to carry up the reaction. It is obvious from the table that the highest benzaldehyde yield (98%) was obtained using ethyl cyanoacetate.

Different solvents including water, acetonitrile, methanol, ethanol, dichloromethane, chloroform, cyclohexane, and toluene were used for the Knoevenagel condensation over P4VP/Al₂O₃-SiO₂(0.6) (in situ). The solvent-free condition was studied as well. The results are summarized in Table 4. It can be seen that both solvent and solvent-free conditions represent good results. The highest yield of 98% was obtained using water as a solvent, indicating the effect of solvent on the reaction product. The solvation energy decreases by increasing polarity of the solvent. This clearly indicates that the reactants, intermediates, and products are more stabilized when polarity of solvent increases [15]. Thus, the reactants, intermediates, and product in water are more stable in comparison to other organic solvents. Solvents play a crucial role in the reaction by stabilizing ionic charges and providing an alternative lower energy pathway with which the reaction may proceed.

The effect of reaction temperature was studied to establish the importance of activation energy in this reaction. Condensation was performed between room temperature and reflux condition (95°C) using P4VP/Al₂O₃-SiO₂(0.6) (in situ) as a catalyst, keeping other parameters constant (Table 5). The percentage of yield surged along with increasing reaction temperature from 63% at room temperature to 98% at 95°C. In general, the Knoevenagel condensation is an endothermic reaction, which indicates that a higher temperature can promote the reaction.

As far as the amount of catalyst is concerned, the variation of catalytic activity was investigated by different amounts of the catalyst, and the results are shown in Figure 5. It is not of practical interest to use a large amount of catalyst. It is observed that while the amount of P4VP/Al₂O₃-SiO₂(0.6) (in situ) increases from 0.02 to 0.04 g, the product yield rises from 92% to 98%. It is because of the availability of more basic sites, which favors the dispersion of more active species. Afterwards, the percentage of yield remains stable at 98% between 0.04 g and 0.12 g. It can be noted that the amount of catalyst used in the Knoevenagel reaction is little. Therefore, in this case, this composite is highly desirable.

FIGURE 5: Effect of catalyst amount on the Knoevenagel condensation over P4VP/Al₂O₃-SiO₂. Reaction conditions: catalyst (P4VP/Al₂O₃-SiO₂(0.6) (in situ)), benzaldehyde (2 mmol), ethyl cyanoacetate (2 mmol), reflux, H₂O (10 mL), reaction time = 30 min, and selectivity = 100%.

In order to investigate the importance of support, the Knoevenagel reaction between benzaldehyde and ethyl cyanoacetate over P4VP/Al₂O₃ and P4VP/SiO₂ was examined under optimum conditions, and the results were compared to P4VP/Al₂O₃-SiO₂ (in situ) (Table 6). As mentioned in previous section, among these three types of catalysts, P4VP/Al₂O₃-SiO₂ (in situ) had the most basic sites. Therefore, it showed the highest yield to the desired product. The activity of Al₂O₃-SiO₂ as a catalyst in the Knoevenagel reaction was also investigated. In this case, the yield of 98% was observed after 30 minutes.

In order to examine the chemoselectivity of the catalyst, equal molar mixtures of ketone (4-nitro acetophenone) and aldehyde (4-nitro benzaldehyde) were allowed to react with ethyl cyanoacetate in water in the presence of the P4VP/Al₂O₃-SiO₂(0.6) (in situ) (Figure 6). The catalyst was able to discriminate between ketone and aldehyde and showed a high chemoselectivity (after five minutes, 100% conversion for 4-nitro benzaldehyde was observed while 4-nitro acetophenone remained unchanged).

In terms of green chemistry, reusability of the catalyst is highly preferable. Hence the recyclability of the catalyst was studied taking P4VP/Al₂O₃-SiO₂(0.6) (in situ) in the repeated experiments. In order to regenerate the catalyst, after the reaction it was separated from the reaction mixture by filtration and washed several times with deionized water and acetone. Then it was dried at 60°C and reused in the other reaction. Interestingly, it was observed that the activity of P4VP/Al₂O₃-SiO₂(0.6) (in situ) did not decrease after four cycles. Therefore, the present catalyst is an interesting candidate for commercial exploitation.

Application of P4VP/Al₂O₃-SiO₂ in Knoevenagel Condensation of Various Aldehydes with Ethyl Cyanoacetate. Knoevenagel condensation of different aldehydes and ethyl cyanoacetate with poly(4-vinylpyridine)/Al₂O₃-SiO₂ (in situ) as a catalyst either in water or solvent-free conditions were investigated (Table 7). The results showed that the aromatic

TABLE 7: Knoevenagel condensation reaction of aromatic and aliphatic aldehydes and ethyl cyanoacetate catalyzed by P4VP/ Al_2O_3 - SiO_2 ^a.

Entry	Substrate	Product	Time (min) ^b	Yield ^c (%)
1			30 (I) 75 (II)	98 98
2			5 (I) 5 (II)	98 98
3			60 (I) 60 (II)	98 70
4			30 (I) 60 (II)	98 90
5			10 (I) 20 (II)	60 40
6			45 (I) 45 (II)	98 60
7			5 (I) 5 (II)	98 98
8			5 (I) 5 (II)	98 98
9			40 (I) 65 (II)	90 87
10			45 (I) 75 (II)	93 93
11			30 (I) 40 (II)	92 90

^a Reaction conditions: catalyst (0.04 g), ethyl cyanoacetate (2 mmol), substrate (2 mmol), H_2O (10 mL), and reflux. ^bFor (I) the solvent was H_2O , and for (II) solvent-free condition was chosen. ^cIsolated yield.

aldehydes, having different substituents such as chloro, nitro, methoxy, and methyl, were converted to the corresponding arylidene derivatives from good to high yields (60% to 98%) in both water and under solvent-free condition. Moreover,

hetero-aromatic aldehydes such as furfural and 4-pyridine carbaldehyde also showed high yield (98%) at very short run (Entries 7 and 8). The aromatic aldehydes with electron-withdrawing groups such as chloro and nitro proceeded at

FIGURE 6: Reaction of 4-nitro acetophenone and 4-nitro benzaldehyde in the presence of the P4VP/Al₂O₃-SiO₂(0.6) (in situ).

faster rates than those with electron-donating groups such as methoxy and methyl. These results showed that electron-donating substituents in aromatic ring appear to retard the rate of reaction due to inactivation of aldehyde group. In addition, the Knoevenagel condensation was carried out using aliphatic aldehydes, which represented the high product yields (Entries 9 to 11). Interestingly, the results clearly established that the obtained products were E-isomer forms.

4. Conclusions

The novel nano-pore heterogeneous basic catalysts were synthesized and characterized by reaction of 4VP in the presence of different supports in various conditions. These new solid basic catalysts become practical alternatives to soluble bases regarding the following advantages: (a) high catalyst activity under mild reaction conditions; (b) easy separation of the catalyst after the reaction; (c) the desirable amount of catalyst; (d) excellent reusability of the catalyst for several repeated experiments. The catalytic activity of the catalyst prepared by in situ method is higher than impregnated method. Therefore, this synthesis method (in situ) can be very suitable for the preparation of composite catalysts.

Acknowledgments

Support from Islamic Azad University, Shahreza Branch (IAUSH) and Research Council and Center of Excellence in Chemistry is gratefully acknowledged.

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