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Research Note

Nano silica phosphoric acid: A suitable catalyst for the synthesis of trisubstituted imidazoles via a sonication condition

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Abstract. Nano silica phosphoric acid has been found to be a suitable catalyst for the preparation of 2,4,5-trisubstituted imidazoles via three-component reactions of benzil, aldehydes and ammonium acetate under a sonication condition.

1. Introduction

Multicomponent reactions (MCRs) have received great interest and are enjoying outstanding status in modern organic synthesis and medicinal chemistry. They are a one-pot process, bringing together three or more components, and show high atom economy and high selectivity [1]. MCRs have made a great contribution to the convergent synthesis of complex and important organic molecules from simple and readily available starting materials, and have emerged as powerful tools for drug discovery [2]. Compounds containing imidazole moiety have many pharmacological properties and play important roles in biochemical processes [3]. The best reported route for synthesis of 2,4,5-trisubstituted imidazoles is condensation of benzil, aldehyde and ammonium acetate in the presence of an acidic catalyst. Recently, some catalysts, such as L-proline [4], K10 [5], zeolite [5], nano sulfated zirconia [5], [EMIM]OAc [6], Zr(acac)$_4$ [7], silica sulfuric acid [8], I$_2$ [9], [Hbim]BF$_4$ [10], InCl$_3$.3H$_2$O [11] and Yb(OTf)$_3$ [12] have been applied to the above mentioned route. Some of the reported protocols have disadvantages, such as harsh reaction conditions, poor yields, prolonged time periods, and the use of hazardous and often expensive acid catalysts. Moreover, the synthesis of these heterocycle compounds has usually been carried out in polar solvents, such as ethanol, methanol, acetic acid, DMF and DMSO, leading to complex isolation and recovery procedures. These processes also generate waste containing catalysts and solvents, which have to be recovered, treated and disposed off. Regarding our research into the synthesis of organic compounds, we wish to report a simple and efficient method for the synthesis of 2,4,5-triarylsubstituted imidazoles in the presence of nano-silica phosphoric acid.

Nano silica phosphoric acid (nano-SPA) [13], as an efficient and reusable catalyst, was prepared by the reaction of nano-silica chloride with dry phosphoric acid. Nano silica chloride was prepared by the reaction

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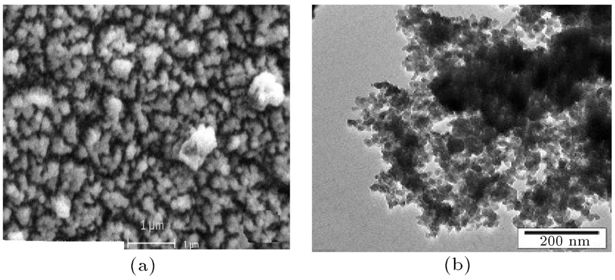
of commercial nano silica gel with thionyl chloride in a reflux condition. The particle size of nano-SPA was measured by SEM and TEM photography (Figure 1).

The acidic capacity of nano-SPA is 10.32 mmol. g^{-1} and was determined via titration of 0.2 g of catalyst, with a standard solution of NaOH.

The FT-IR (ATR) spectra of silica chloride, nano-SPA and $H_3PO_4.SiO_2$ are shown in Figure 2. In some ATR spectra, the Si-O-H and Si-O-Si stretching bands appear in the range of 900-1100 cm^{-1}. In the silica chloride spectrum, the Si-Cl stretching band appears in 700 cm^{-1}. In ATR spectra of nano-SPA and $H_3PO_4.SiO_2$, the P-O-H, P=O, P-O stretching bands appear at 910-1040, 1637 and 2400-2800 cm^{-1}, respectively. Therefore, the structural of nano-SPA is suggested in Scheme 1.



(a) (b)

Figure 1. a) SEM and b) TEM photograph of nano-SPA.

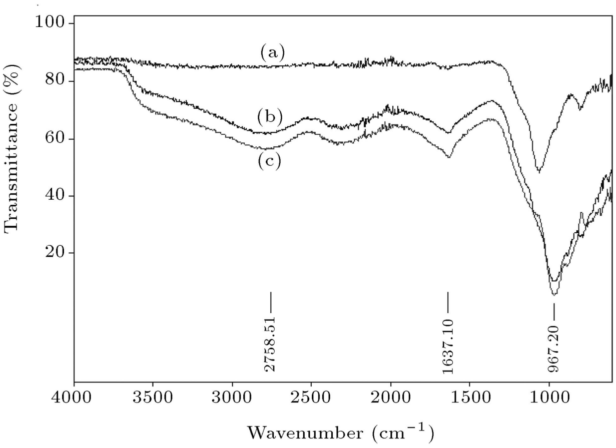
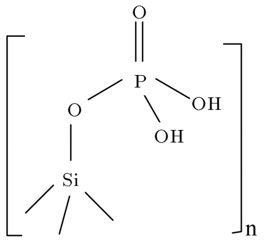


Figure 2. ATR of a) silica chloride, b) nano-SPA and c) $H_3PO_4.SiO_2$.



Scheme 1. A proposed structure for nano SPA.

The X-Ray Diffraction (XRD) patterns of nano-SiO_2 and nano-SPA are shown in Figure 3. The nano-SiO_2 XRD pattern has a strong peak in the 2θ value of 21.8024° and FWHM equal to 1771, and the nano-SPA XRD pattern has a strong broad peak in 21.718 and FWHM equal to 2.3616. According to the Scherrer equation, the broadening of peaks or high Full Width at Half Maximum (FWHM) value means a decrease in the particle size of nano-SPA.

2. Results and discussion

To find the optimum condition for the synthesis of 2,4,5-trisubstituted imidazoles in the presence of SPA, we have synthesized 2,4,5-triphenyl imidazole in the presence of SPA under various conditions (Table 1). As seen, in conventional thermal conditions, such as 45-120°C in different solvents, poor yields were obtained (Table 1, entries 1-9). Meanwhile, the mixing of neat materials in a mixer mill apparatus did not afford a good yield (Table 1, entry 10). The ultrasonic assisted synthesis of the presented reaction was studied using SPA or nano-SPA in ethyl acetate under reflux conditions (Table 1, entries 11 and 12). It was found that under sonication conditions, the reaction time decreased to 30 minutes. Reactions at different

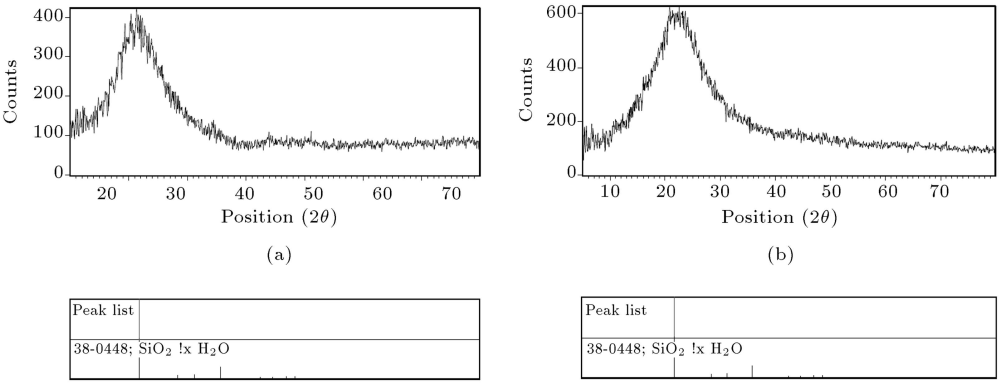
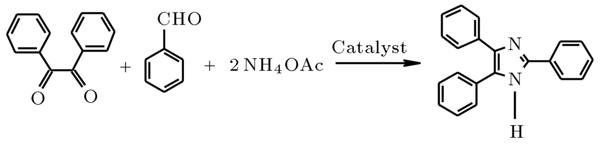


Figure 3. X-Ray Diffraction (XRD) pattern of a) nano SiO_2 and b) nano-SPA.

Table 1. Synthesis of 2,4,5-triphenyl imidazole using SPA or nano-SPA under different conditions[a].

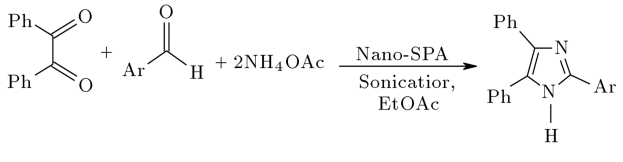


Entry	Catalyst (g)	Solvent	Condition	Time (h)	Yield (%)	Ref.
1	SPA (0.05)	-	120°C	3	60	-
2	SPA (0.06)	-	120°C	3	50	-
3	SPA (0.06)	DMSO	110°C	3	86	-
4	SPA (0.06)	CH_2Cl_2	45°C	24	20	-
5	SPA (0.06)	*n*-Hexan	50°C	24	50	-
6	SPA (0.06)	EtOH	75°C	6	48	-
7	SPA (0.06)	HOAc	80°C	24	50	-
8	SPA (0.06)	MeOH	65°C	6	46	-
9	SPA (0.06)	Isopropanol	82°C	6	45	-
10	SPA (0.06)	-	Mixer mill	0.5	60	-
11	SPA (0.06)	Ethyl acetate	Ultrasound/reflux.	0.5	80	-
12	Nano-SPA (0.01)	Ethyl acetate	Ultrasound/reflux.	0.5	92	-
13	Nano-SPA (0.01), 2nd run	Ethyl acetate	Ultrasound/reflux.	0.6	75	-
14	Nano-SPA (0.01), 3rd run	Ethyl acetate	Ultrasound/reflux	0.6	60	-
15	L-Proline	MeOH	60°C	9	90	[4]
16	Zeolite	EtOH	Reflux	1	80	[5]
17	K10	EtOH	Reflux	1.5	70	[5]
18	Nano -sulfated zirconia	EtOH	Reflux	0.7	87	[5]
19	[EMIM]OAc	EtOH	Ultrasound/r.t.	0.7	87	[6]
20	$Zr(acac)_4$	EtOH	Ultrasound/r.t.	0.5	94	[7]
21	$Zr(acac)_4$	EtOH	Reflux	2.5	90	[7]
22	SSA	-	130°C	0.8	83	[8]
23	SSA	-	mw	0.2	85	[8]
24	I_2	EtOH	75°C	0.25	99	[9]
25	[Hbim]BF4	-	100°C	0.5	93	[10]
26	$InCl_3.3H_2O$	MeOH	r.t	12	73	[11]
27	-	PEG-400	110°C	1/5	88	[14]
28	$Yb(OTf)_3$	HOAc	70°C	2	92	[12]

[a]: The molar ratio of benzaldehyde: benzil: ammonium acetate: SPA (g) equal to 1:1: 2:0.06.

temperatures and various molar ratios of substrates in the presence of nano-SPA revealed that the best conditions were sonication and a ratio of aldehyde (mmol): benzil (mmol): ammonium acetate (mmol): nano-SPA (g) equal to 1:1:2:0.01. The reusability of the nano-SPA catalyst was also examined. After each run, the product was filtered, the solvent evaporated, the catalyst washed with $CHCl_3$, and reused. Treatment with $CHCl_3$ removes tars more efficiently from the catalyst surface (Table 1, entries 13 and 14). The catalyst was reusable, although a gradual decline in activity was observed.

Therefore, various aldehydes was used as substrates for the synthesis of 2,4,5-trisubstituted imidazoles derivatives under a sonication condition (Scheme 2 and Table 2).



Scheme 2. Synthesis of 2,4,5-trisubstituted imidazoles in the presence of nano-SPA under sonication condition.

In conclusion, we have demonstrated a simple method for the synthesis of 2,4,5-trisubstituted imidazoles using nano-SPA as a reusable, eco-friendly, inexpensive and efficient catalyst. Short reaction times,

Table 2. Nano-SPA catalyzed synthesis of 2,4,5-trisubstituted imidazoles under sonication condition[a].

Entry	Ar	Yield (%)[b]	M.P.°C (lit.)	Ref.
1	C_6H_5	92	274 (274-275)	[6]
2	4-CH_3-C_6H_4	85	236 (227-229)	[14]
3	4-NO_2-C_6H_4	72	240(239-242)	[6]
4	4-Cl-C_6H_4	83	261(260-262)	[5]
5	2-OMe-C_6H_4	90	210(210-211)	[4]
6	4-OMe-C_6H_4	91	230(230-231)	[7]
7	2-Cl-C_6H_4	80	186(188)	[10]
8	2,4-Cl_2-C_6H_3	83	175(174-175)	[7]
9	4-Br-C_6H_4	82	254(254-256)	[5]
10	2-NO_2-C_6H_4	89	230(230-231)	[4]
11	3-NO_2-C_6H_4	90	> 300(> 300)	[14]
12	4-OH-C_6H_4	91	267(265-267)	[14]
13	2-Br-C_6H_4	82	201(201-202)	[6]

[a]: A mixture of benzil (1 mmol): aldehyde (1 mmol): ammonium acetate (1 mmol): and nano SPA (0.01 g) in ethylacetate was sonicated under power 100 watts for 30 minutes.

[b]: Isolated yield.

high yields, simplicity of the operation and easy work-up are some advantages of this method.

3. Experimental

3.1. General

The materials were purchased from Merck Company and were used without any additional purification. Meanwhile, commercial nano silica gel with pore size of 20 nm was purchased from the Aldrich Company. Products were characterized by FT-IR, ^{1}H-NMR, and a comparison of their physical properties with those reported in the literature. FT-IR (ATR) spectra were run on a Bruker, Eqinox 55 spectrometer. A Bruker (DRX-400 Avanes) NMR was used to record the ^{1}H NMR spectra.The SEM of nano particles was determined with a VEGA/TESCAN scanning electron microscope and a TEM photograph was prepared using a 912AB OMEGA microscope. A BANDELIN Sonopulse HD 3200 ultrasonic apparatus was used for sonication.

3.2. Preparation of nano silica phosphoric acid (nano-SPA)

Thionyl chloride (20 mL) was added to an oven-dried (120°C) nano silica gel (1 g) in a round bottomed flask (50 mL) equipped with a condenser and a drying tube, and refluxed for 48 h. The excess thionyl chloride was distilled off and the resulting white-grayish powder (named nano silica chloride (nano-SC)) was dried and used as starting material for the preparation of nano-SPA. In the next step, anhydrous H_3PO_4 (0.98 g, 0.01 mol) was added to a suspension of nano-SC (0.94 g) in CH_2Cl_2 (20 mL) and stirred vigorously for 2 h. Then, the reaction mixture was filtered and the residue washed with CH_2Cl_2 (2×5 mL). Nano-SPA was obtained as a white powder.

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

A mixture of benzil (1 mmol), aldehyde (1 mmol), ammonium acetate (2 mmol), nano-SPA (0.01 g) in 5 ml ethylacetate was sonicated for 30 minutes. The progress of the reaction was followed by TLC. After completion of the reaction and evaporation of ethylacetate, the mixture was cooled to room temperature. $CHCl_3$ was added to the mixture which was filtered to remove the catalyst. After evaporation of the solvent, an oily residue or an impure solid was obtained. By adding ethanol and water to the residue, a milky to yellow solid was obtained. The solid was then crystallized from ethanol.

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References

1. Cariou, C.C.A., Clarkson, G.J. and Shipman, M. "Rapid synthesis of 1,3,4,4-tetrasubstituted β-Lactams from methylene aziridines using a four-component reaction", *J. Org. Chem.*, **73**, pp. 9762-9764 (2008).
2. Kalinski, C., Lemoine, H., Schmidt, J., Burdack, C., Kolb, J., Umkehrer, M. and Ross, G. "Multicomponent reactions as a powerful tool for generic drug synthesis", *Synlett*, **24**, pp. 4007-4011 (2008).
3. Lambardino, J.G. and Wiseman, E.H. "Preparation and anti inflammatory activity of some nonacidic trisubstituted imidazoles", *J. Med. Chem.*, **17**, pp. 1182-1188 (1974).
4. Samai, S., Nandi, G.C., Singh, P. and Singh, M.S. "L-Proline: an efficient catalyst for the one-pot synthesis of 2,4,5-tri-substituted and 1,2,4,5-tetra-substituted imidazoles", *Tetrahedron*, **65**, pp. 10155-10161 (2009).
5. Teimouri, A. and Najafi Chermahini, A. "An efficient and one-pot synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles catalyzed via solid acid nano-catalyst", *J. Mol. Catal. A: Chem.*, **346**, pp. 39-45 (2011).
6. Zang, H., Su, Q., Mo, Y., Cheng, B.W. and Jun, S. "Ionic liquid [EMIM]OAc under ultrasonic irradiation towards the first synthesis of tri-substituted imidazoles", *Ultrason. Sonochem.*, **17**, pp. 749-751 (2010).
7. Khosropour, A.R. "Ultrasound-promoted greener synthesis of 2,4,5-tri-substituted imidazoles catalyzed by $Zr(acac)_4$ under ambient conditions", *Ultrason. Sonochem.*, **15**, pp. 659-664 (2008).

8. Shaabani, A., Rahmati, A., Farhangi, E. and Badri, Z. "Silica sulfuric acid promoted the one-pot synthesis of tri-substituted imidazoles under conventional heating conditions or using microwave irradiation", *Catal. Commun.*, **8**, pp. 1149-1152 (2007).
9. Kidwai, M., Mothsra, P., Bansal, V., Somvanshi, R.K., Ethayathulla, A.S., Dey, S. and Singh, T. "One-pot synthesis of highly substituted imidazoles using molecular iodine: A versatile catalyst", *J. Mol. Catal A: Chem.*, **265**, pp. 177-182 (2007).
10. Siddiqui, S.A., Narkhede, U.C., Palimkar, S.S., Daniel, T., Lahoti, R.J. and Srinivasan, K.V. "Room temperature ionic liquid promoted improved and rapid synthesis of 2,4,5-triaryl imidazoles from aryl aldehydes and 1,2-diketones or α-hydroxyketone", *Tetrahedron*, **61**, pp. 3539-3546 (2005).
11. Sharma, S.D., Hazarika, P. and Konwar, D. "An efficient and one-pot synthesis of 2,4,5-tri-substituted and 1,2,4,5-tetra-substituted imidazoles catalyzed by $InCl_3$. $3H_2O$", *Tetrahedron Lett.*, **49**, pp. 2216-2220 (2008).
12. Min, L., Wang, Y.H., Tian, H., Yao, Y.F., Shao, J.H. and Liu, B., "Ytterbium triflate as an efficient catalyst for one-pot synthesis of substituted imidazoles through three-component condensation of benzil, aldehydes and ammonium acetate", *J. Fluorine Chem.*, **127**, pp. 1570-1573 (2006).
13. Zolfigol, M.A., Shirini, F., Zamani, K., Ghofrani, E., and Ebrahimi, S. "Silica phosphoric acid/$NaNO_2$ as a novel heterogeneous system for the coupling of thiols to their corresponding disulfides", *Phosphorus Sulfur*, **179**, pp. 2177-2182 (2004).
14. Wang, X.C., Gong, H.P., Quan, Z.J., Li, L. and Ye, H.L. "PEG-400 as an efficient reaction medium for the synthesis of 2,4,5-triaryl-1H-imidazoles and 1,2,4,5-tetra-aryl-1H-imidazoles", *Chinese Chem. Lett.*, **20**, pp. 44-47 (2009).

Biographies

Abdolhamid Bamoniri was born in Abadan, Iran, in 1958. He obtained a BS degree in Chemistry from Shahid Beheshti University, Tehran, Iran, in 1984, a MS degree in Organic Chemistry from Tarbiat Moalem University, Tehran, Iran, in 1989, and a PhD degree in Organic Chemistry from Bu-Ali Sina University, Hamadan, Iran, in 2003. He is currently Associate Professor at the University of Kashan, Iran.

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