Short communication

Synthesis of 2,4,5-Trisubstituted Phenanthroimidazole Derivatives using SBA-Pr-SO₃H as a Nanocatalyst

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Abstract

An efficient one-pot approach for the preparation of 2,4,5-trisubstituted phenanthroimidazole derivatives is described. The three-component reaction between 9,10-phenanthraquinone, benzaldehyde derivatives, and ammonium acetate proceeds in the presence of SBA-Pr-SO₃H as a nanoporous solid acid catalyst in short reaction times and good to excellent yields.

Keywords: Trisubstituted phenanthroimidazole; 9,10-Phenanthraquinone; SBA-Pr-SO₃H; Nanocatalyst; Heterogeneous catalysis

1. Introduction

Application of imidazole and their derivatives is unavoidable in the field of medicinal chemistry due to their biologically active properties as biocides,¹ platelet aggregation inhibitors,² analgetics,³ antibacterial,^{4,5} antitumor,^{6,7} and anti-inflammatory activity.^{8,9} Additionally, derivatives of imidazole conjugated with aromatic rings have been widely used as fluorescent dyes.¹⁰

In recent years, several methods have been reported for the preparation of three-substituted imidazole derivatives from 9,10-phenanthraquinones, benzaldehyde derivatives and ammonium acetate using different catalysts such as I₂,¹¹ mercaptopropylsilica,¹² zirconium Schiff base,¹³ iron(III) triflate,¹⁴ sulfamic acid,¹⁵ and ionic liquid modified surface.¹⁶

Recently, mesoporous ordered silica materials such as SBA-15 have received more attention in the field of catalysis.^{17,18} As a well ordered hexagonal mesoporous silica, SBA-15 has relevant characteristics such as large uniform pore size, high surface area, thick walls, and high thermal stability which makes it a good candidate for preparing organic-inorganic hybrid materials and using as catalyst in different reactions.¹⁹ Furthermore, the propyl sulfonic acid modified SBA-15 can behave as an efficient

Brønsted acid in organic synthesis. Due to our interest in the field of nano-heterogeneous acidic catalysts,^{20–23} and based on different studies on applying SBA-Pr-SO₃H in organic synthesis,^{24–30} we have discovered a green and efficient method for the synthesis of 2,4,5-trisubstituted phenanthroimidazoles **4a-i** using SBA-Pr-SO₃H. In our previous studies, we have already reported the efficient synthesis of benzimidazoquinazolinones³¹ and 1,2,4,5-tetrasubstituted imidazoles³² in the presence of SBA-Pr-SO₃H.

2. Experimental

2.1. Materials and Instrumentations

All chemicals were obtained commercially and used without further purification. The IR spectra were recorded on KBr disks using a FT-IR Bruker Tensor 27 instrument. Melting points were measured using the capillary tube method with an Electrothermal 9200 apparatus. ¹H NMR and ¹³C NMR spectra were obtained by a Bruker 400 MHz and 100 MHz spectrometer, respectively, in either DMSO-*d*₆ or CDCl₃ solution. Mass spectra data were obtained by using a Network mass selective detector 5973 (Agilent). Scanning electron microscope (SEM) analysis

was performed on a Philips XL-30 field-emission SEM operated at 16 kV, while TEM was carried out on a Tecnai G² F30 apparatus at 300 kV. Weight change curve in nitrogen was measured on a BAHF Thermo analyser STA 503 with the maximum heating rate of 20 °C/min.

2. 2. General Procedure for the Synthesis of 2,4,5-trisubstituted phenanthroimidazoles (4a–i)

The mixture of 9,10-phenanthraquinone (0.20 g, 1 mmol), benzaldehyde derivatives (1 mmol), and ammonium acetate (0.31 g, 4 mmol) was stirred in refluxing acetic acid (3 mL) for about 30 min using SBA-Pr-SO₃H (0.02 g) as the catalyst. The completion of the reaction was monitored by TLC technique (ethyl acetate/petroleum ether, 2:1). The precipitated product was filtered and dissolved in hot ethanol and DMF to remove the catalyst, and the solvent evaporated to obtain the pure product. The catalyst was subsequently washed with a diluted hydrochloric acid solution, distilled water, acetone and dried under reduced pressure, and reused for several times without significant loss of catalytic activity.³³ Physical and spectroscopic data of two new compounds are given below.

2. 3. Spectral Data of New Products

2-(2,4-Dimethoxyphenyl)-1*H*-phenanthro[9,10-*d*]imidazole (4h)

IR (KBr, ν_{max}): 3523, 3430, 3048, 2987, 2942, 2833, 1935, 1603, 1462, 1371, 1311, 1266, 1204, 1161, 1083, 1022, 923, 835, 747, 714, 564, 434 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 3.87 (s, 3H, CH₃), 4.03 (s, 3H, CH₃), 6.76 (dd, 1H, *J*=11.5 Hz, *J*=3 Hz, ArH), 6.80 (d, 1H, *J*=2.8 Hz, ArH), 7.58–7.74 (m, 4H, ArH), 8.20 (d, 1H, *J*=11.4 Hz, ArH), 8.62 (d, 1H, *J*=10.4 Hz, ArH), 8.70 (d, 1H, *J*=10.5 Hz, ArH), 8.82 (t, 2H, *J*=10.8 Hz, ArH), 12.57 (s, 1H, NH) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆) δ : 55.5, 55.9, 98.5, 105.9, 111.8, 111.9, 121.9, 122.4, 122.5, 123.7, 123.9, 125, 126.6, 126.8, 126.9, 127, 127.3, 127.4, 131.1, 136.2, 147.3, 157.8, 161.6 ppm. MS (*m/z*, %): 354 (M⁺, 100), 336(33), 321(47), 309(23), 267(24), 190(20), 177(28), 163(13), 137(22).

2-(2,6-Dichlorophenyl)-1*H*-phenanthro[9,10-*d*]imidazole (4i)

IR (KBr, ν_{max}): 3063, 2973, 2904, 2845, 2737, 1948, 1702, 1602, 1548, 1481, 1437, 1327, 1191, 1153, 1041, 954, 880, 784, 740, 617, 531, 432 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 7.60–7.75 (m, 7H, ArH), 8.36 (d, 1H, *J*=10.4 Hz, ArH), 8.56 (d, 1H, *J*=10.3 Hz, ArH), 8.81–8.88 (m, 2H, ArH), 13.82 (s, 1H, NH) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆) δ : 121.7, 122, 122.4, 123.8, 124.2, 125.3, 125.6, 127.1, 127.14, 127.3, 127.5, 127.8, 128.4, 130.7, 132.5, 135.7, 136.5, 144.2 ppm. MS (*m/z*, %): 362 (M⁺, 100), 336(9), 190(86), 171(18), 163(53), 136(18).

3. Results and Discussion

The reaction of 9,10-phenanthraquinone (**1**), 4-chlorobenzaldehyde (**2a**), and ammonium acetate (**3**) was selected for optimizing conditions and investigating the role of nanocatalyst, SBA-Pr-SO₃H (Scheme 1). In order to study the solvent effect, different solvents were tested including solvent-free system at ambient temperature and at 120 °C, refluxing in water, ethanol and/or acetic acid as green solvents. As shown in Table 1, the best yield was obtained under refluxing in acetic acid in the presence of SBA-Pr-SO₃H (0.02 g). On the other hand, to indicate the catalyst effect, the results of different catalysts were compared with SBA-Pr-SO₃H under modified conditions (Figure 1). Clearly, SBA-Pr-SO₃H led to both, shorter reaction times and higher yields. After optimizing the reaction conditions, several aromatic aldehydes were used for the synthesis of 2,4,5-trisubstituted phenanthroimidazoles (Figure 2), which are listed in Table 2.

The proposed mechanism is shown in Scheme 2. In the first step, aldehyde carbonyl group is protonated on the SBA-Pr-SO₃H surface acidic sites. The activated carbonyl group is susceptible to the nucleophilic attack of ammonia, produced from the ammonium acetate (**3**), and gives the intermediate (**4'**). Condensation of 9,10-phenanthraquinone (**1**) with intermediate **4'** through an imination process and proton replacement in intermediate **4''**, produces the desired products **4a–i**.

Scheme 1. Model reaction of 9,10-phenanthraquinone **1**, 4-chlorobenzaldehyde **2a**, and ammonium acetate **3** for the synthesis of **4a**.

Table 1: Optimizing the reaction conditions for the synthesis of **4a**.

Entry	Catalyst	Solvent	Condition	Time (min)	Yield (%)
1	SBA-Pr-SO ₃ H	—	r.t.	24 h	Trace
2	SBA-Pr-SO ₃ H	—	120 °C	N. R.	80
3	SBA-Pr-SO ₃ H	H ₂ O	Reflux	>5 h	—
4	SBA-Pr-SO ₃ H	EtOH	Reflux	>5 h	73
5	SBA-Pr-SO ₃ H	CH ₃ COOH	Reflux	5	95
6	—	CH ₃ COOH	Reflux	10	90

Figure 1. Comparison of reaction times and product yields for the synthesis of **4** using different catalysts including I₂,¹¹ mercaptopropylsilica (MPS),¹² *p*-toluenesulfonic acid (*p*-TSA),¹³ NH₂SO₃H,¹⁵ supported ionic liquid-like phase (SILLP),¹⁶ and SBA-Pr-SO₃H. **Figure 2.** Schematic synthesis of 2,4,5-trisubstituted phenanthroimidazoles (**4**).**Scheme 2.** The proposed mechanism for the synthesis of 2,4,5-trisubstituted phenanthroimidazoles (**4**).

SBA-15 was synthesized according to the reported method.³³ Then, its internal surface was modified by using (3-mercaptopropyl)trimethoxysilane, and further oxidation with H₂O₂ in methanol, producing SBA-Pr-SO₃H, which was characterized *via* different techniques, including TGA, SEM and TEM analysis. The

weight reduction in TGA analysis (Figure 3) in the temperature range of 200–600 °C, indicates that propyl sulfonic acid groups were grafted onto the pores of silica material and that the average amount is 1.2 mmol/g. The mass loss before 200 °C is due the adsorbed water onto the pores of SBA-Pr-SO₃H. SEM image of SBA-

Table 2: Synthesis of 2,4,5-trisubstituted phenanthroimidazoles (**4**) in the presence of SBA-Pr-SO₃H under reflux conditions in acetic acid.^a

Entry	R	Product	Time (min)	Yield (%)	mp (°C)	mp (Lit.)
1	4-Cl		10	95	263–265	275–276 ¹⁴
2	4-F		20	96	205–208	–
3	4-OMe		10	95	265–267	265–257 ³⁴
4	4-Me		10	97	292–295	290–292 ³⁵
5	4-OH		20	97	>300	350–352 ¹⁴
6	3-NO ₂		20	90	278–280	271–272 ³⁶
7	2,4-(Cl) ₂		10	94	242–244	245–246 ¹⁵
8	2,4-(OMe) ₂		20	93	203–205	New
9	2,6-(Cl) ₂		20	90	230–232	New

^a Typical reaction conditions: 9,10-phenanthraquinone (1 mmol), benzaldehyde (1 mmol), and ammonium acetate (4 mmol) in the presence of SBA-Pr-SO₃H (0.02 g) were stirred in refluxing acetic acid (3 mL).

Figure 3. TGA curve of SBA-Pr-SO₃H.

Figure 4. The SEM (left) and TEM (right) images of SBA-Pr-SO₃H.

Pr-SO₃H showed same morphology as obtained for SBA-15, proving this process didn't change the structure of SBA-15 itself (Figure 4). TEM image also demonstrated the presence of channels onto the SBA-Pr-SO₃H structure which were not collapsed after modification.

4. Conclusion

In conclusion, we have developed a novel three-component reaction to prepare 2,4,5-trisubstituted phenanthroimidazoles (**4**) from 9,10-phenanthraquinones, benzaldehyde derivatives and ammonium acetate. High yields, mild reaction conditions, simple purification, and the ability to recycle the heterogenous nanocatalyst, SBA-Pr-SO₃H, make this method an ecologically friendly for the synthesis of **4**. This protocol expands the new pathways for employing green catalysts to design other similar multicomponent reactions.

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6. References

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Povzetek

V prispevku je predstavljena učinkovita enostopenjska reakcija priprave 2,4,5-trisubstituiranih fenantroimidazolnih derivatov. Trikomponentna reakcija med 9,10-fenantrokinonom, različnimi derivati benzaldehda in amonijevim acetatom, v prisotnosti SBA-Pr-SO₃H kot trnega, nanoporoznega kislega katalizatorja, poteka hitro, s kratkimi reakcijskimi časi in odličnimi izkoristki.