



Research Journal of Pharmaceutical, Biological and Chemical Sciences

SnCl₂·2H₂O catalyzed one-pot synthesis of 2-phenylimidazo [4, 5-*f*] [1, 10] phenanthroline

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ABSTRACT

Various 2-phenylimidazo [4, 5-*f*] [1, 10] phenanthrolines were synthesized from SnCl₂·2H₂O catalyzed three component reaction of 1, 10-phenanthroline-5, 6-dione, aromatic aldehydes and ammonium acetate at room temperature in excellent isolated yield. This is a simple and straight forward, high yielding, not involving any hazardous or expensive catalyst method.

Keywords: 2-Phenylimidazo [4, 5-*f*] [1, 10] phenanthrolines, Aromatic aldehyde, SnCl₂·2H₂O, Ammonium acetate

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INTRODUCTION

Imidazoles are heterocycles with a wide range of applications and are receiving growing attention [1]. The imidazole ring system is of particular interest because it is a component of histidine and its decarboxylation metabolite histamine [2]. The potency and wide applicability of the imidazole pharmacophore can be attributed to its hydrogen bond donor-acceptor capability as well as its high affinity for metals, which are present in many protein active site [3] (e.g. Zn, Fe, Mg). Also, improved pharmacokinetics and bioavailability of peptide based protease inhibitors have been observed by replacing an amide bond with imidazoles [4]. In addition, the substituted imidazole ring systems are substantially used in ionic liquids [5] that have been given a new approach to "Green Chemistry". Due to their great importance, many synthetic strategies have been developed. In 1882, Radziszewski and Japp reported the first synthesis of the imidazoles from 1, 2-dicarbonyl compound, various aldehydes and ammonia to obtain the imidazoles [6, 7]. Also Siddiqui et al. proposed the synthesis of the imidazole using ionic liquids [8]. Recently, there are several methods reported in the literature for the synthesis of imidazoles using Zeolite HY/silica gel [9], $ZrCl_4$ [10], $NiCl_2 \cdot 6H_2O$ [11], iodine [12], sodium bisulfite [13], acetic acid [14]. However these methods require prolonged reaction time and exotic reaction condition. Thus, the development of a new method for the synthesis of imidazoles derivatives would be highly desirable.

Multi-component condensations (MCCs) constitute an especially attractive synthesis strategy for rapid and efficient generation of molecules due to the fact that the products are formed in a single step and also the diversity could be achieved simply by varying the reacting components. In recent years, $SnCl_2 \cdot H_2O$ have gained special attention as a catalyst in organic synthesis because $SnCl_2 \cdot H_2O$ is widely used as a reducing agent and Lewis acid catalyst [15], many advantages such as excellent solubility in water, uncomplicated handling, inexpensiveness and eco-friendly nature. Recently, several synthetically useful organic transformations using $SnCl_2 \cdot H_2O$ as a catalyst have been reported in the literature. Herein, we were used $SnCl_2 \cdot 2H_2O$ as a catalyst, it has gained a vast importance in organic synthesis due to their several advantages such as, operational simplicity, no toxicity, reusability, low cost, and ease of isolation after completion of the reaction.

EXPERIMENT

General procedure for the synthesis of 2-phenylimidazo [4, 5-f] [1, 10] phenanthrolines 3(a-m)

A mixture of aromatic aldehyde (1 mmol), 1, 10-phenanthroline-5, 6-dione (1 mmol) ammonium acetate (5 mmol), and $SnCl_2 \cdot 2H_2O$ (15 mol %) were ground together in a mortar with a pestle at room temperature for appropriate time in Table 2. After completion of reaction confirmed by TLC, the mixture was treated with water to furnish the crude products. The crude was further purified by column chromatography by using petroleum ether: ethyl acetate (9:1) eluent and get the corresponding 2-Phenylimidazo [4, 5-f] [1, 10] phenanthrolines 3(a-m). The

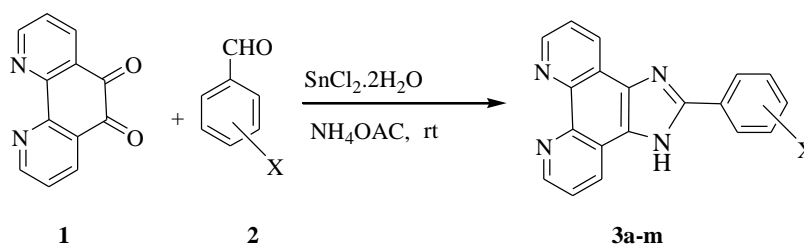
products **3(a-m)** were confirmed by comparison with authentic sample, IR, ^1H NMR, mass, elemental analysis and melting points.

4-(1H-Imidazo [4, 5-f] [1, 10] phenanthroline-2-yl) Phenol (3c): pale yellow solid; mp. 300 $^{\circ}\text{C}$, IR (KBr, cm^{-1}): 3392 (stretch OH); ^1H NMR (90MHz, CDCl_3 DMSO- d_6): δ 13.31, (br.s, 1H), 9.72, (s, 1H), 9.05, (d, 2H), 8.92, (d, 2H), 8.13, (d, 2H), 7.73, (dd, 2H), 6.97, (d, 2H); LS-MS: m/z = 313 (M^+); Anal. Calcd for $(\text{C}_{19}\text{H}_{12}\text{N}_4\text{O})_2(\text{H}_2\text{O})_3$: C, 67.24; H, 4.45; N, 16.51%. Found: C, 67.20; H, 4.61; N, 16.07%.

2-(4-Nitrophenyl)-1H-imidazo[4,5-f][1,10]phenanthroline (3d): pale yellow solid; mp. 302 $^{\circ}\text{C}$, IR (KBr, cm^{-1}): 3397, 3108, 1606, 1541, 1384, 1198, 739; ^1H NMR (90MHz, CDCl_3 DMSO- d_6): δ 13.92, (br. s, 1H), 9.07, (d, 2H), 8.94, (d, 2H), 8.53, (d, 2H), 8.39, (d, 2H), 7.78, (dd, 2H); GC-MS: m/z = 342 (M^+).

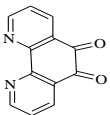
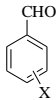
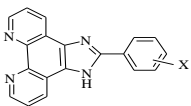
RESULTS AND DISCUSSION

As a part of our ongoing investigation in developing a versatile and efficient method for synthesis of heterocycles compounds[16-19] herein, we report efficient synthetic method for the synthesis of 2-phenylimidazo [4, 5-f] [1, 10] phenanthrolines from 1, 10-phenanthroline-5, 6-dione, substituted aromatic aldehyde and ammonium acetate in the presence of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (**Scheme1**).



Scheme 1. Synthesis of 2-phenylimidazo [4, 5-f] [1, 10] phenanthroline **3(a-m)**.

Table 1. $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ catalyzed synthesis of 1, 10 phenanthroline-5, 6-diones

Entry	Ketones 1	Aldehydes 2	Products 3(a-m)	Yield ^{a,b} (%)
1			 X= a. H; b. 4-Cl; c. 4-OH; d. 4- NO_2 ; e. 2-OH; f. 3- NO_2 ; g. 2- NO_2 ; h. 4-CN; i. 4-OMe; j. 2,4,6-OMe; k. 4-N(Me) $_2$	3a ,93; 3b , 91; 3c , 90; 3d , 90; 3e , 93; 3f , 89; 3g , 85; 3h , 84; 3i , 81; 3j , 90; 3k , 91;

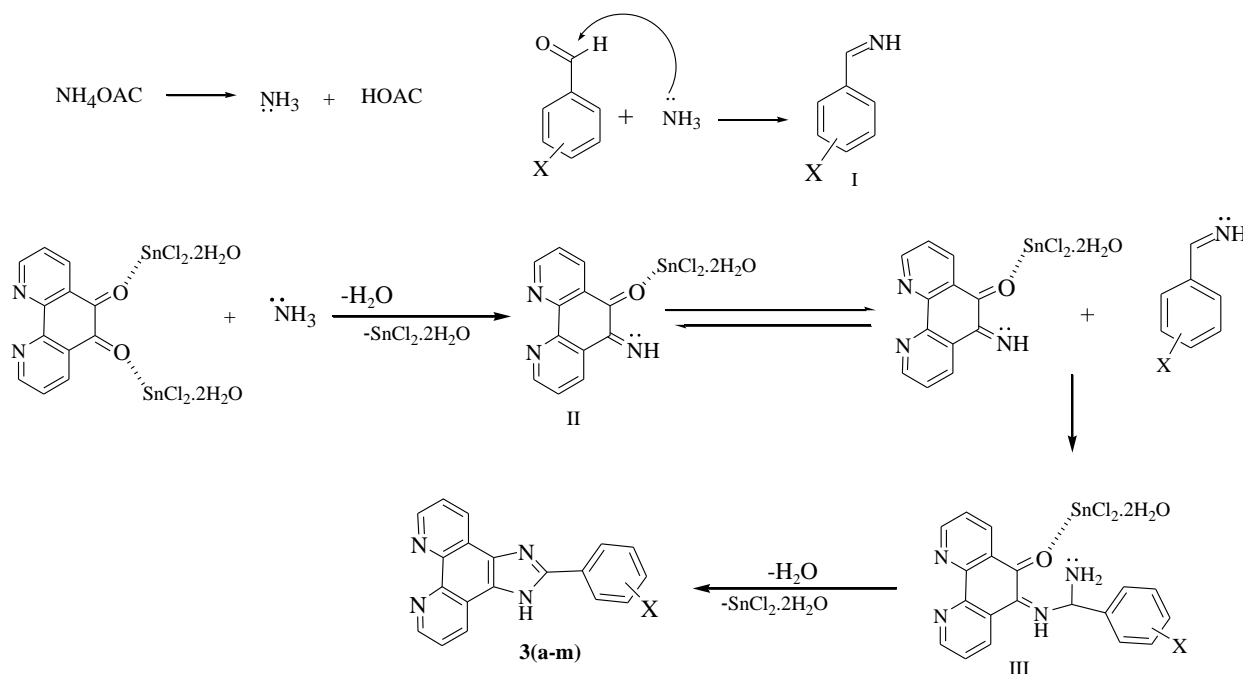
^aYield of isolated pure products. ^bproducts were characterized by IR, NMR, Mass elemental analysis and comparison with authentic sample.

Table 2. Optimization of catalytic concentration on the 3a X-H under solvent free conditions

Entry	Time (min)	Yield (%)*	SnCl ₂ .2H ₂ O (mol %)
1	20	00	No
2	10	traces	01
3	07	20	02
4	05	85	05
5	03	93	10
6	03	93	15

* Isolated yield after column chromatography.

Reaction was carried out simply by mixing 1, 10-phenanthroline-5, 6-dione with an aromatic aldehyde, ammonium acetate in the presence of a catalytic amount 15 mol % of SnCl₂.2H₂O under solvent free condition. The mixture was ground to gather in a mortar with a pestle at room temperature for short reaction time, and then purified by column chromatography, substituted imidazole derivatives were obtained in excellent yields. Accordingly, (10 mol %) of catalyst was sufficient to catalyze the reaction. A rate enhancement with high yield was observed when higher molar ratios of SnCl₂.2H₂O were used. However no product formation was observed in absence of SnCl₂.2H₂O. By getting this result, we have extended this protocol to a variety of aldehydes and Ketones summarized in Table 1. This protocol is rapid and efficient for the preparation of several substituted imidazoles from both electrons efficient as well as electron deficient aromatic aldehydes. There is no effect on electron-withdrawing group and electron-donating group on reaction yield time. When aliphatic aldehyde and Ketones (e.g. acetaldehyde, acetone) were also used as starting carbonyl compounds for the same reaction, no products formation took place in this reaction by grinding the reagents after extensive time more than 30 minutes. Different the *ortho* and *para* phenyl group substituents did not show any effect on the formation rate of imidazoles. However, *meta* substitution requires somewhat greater time as compared to the *o/p* substituents. Heteroaromatic Ketones reacted fast and gave excellent yields of desired imidazoles. A nearly stoichiometric amount of ammonium acetate was used in the course of the reaction, where as previously a many-fold excess of ammonium acetate was required. This is an additional advantage of the novel methodology. The possible mechanism of this reaction is shown in (Scheme 2). The SnCl₂.2H₂O increase the electrophilic character of aromatic aldehyde towards the ammonia to give the imines as intermediate I. Further catalyst SnCl₂.2H₂O condenses with the carbonyl oxygen's of the ketone, which on dehydration afford the intermediate II. Intermediates I and II combine for the formation of intermediate III, which on dehydration and further cyclisation afford the corresponding desired products (Scheme 2).



CONCLUSION

The $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ has been employed as a novel, mild, and very efficient catalyst for the convenient synthesis of 2-phenylimidazo [4, 5-f] [1, 10] phenanthrolines in excellent yields from wide variety of aldehyde. In addition, low-cost of catalyst, solvent-free conditions, environmental friendliness, easy availability, make this methodology a valid contribution to the existing processes in the field of 2-phenylimidazo [4, 5-f] [1, 10] phenanthrolines derivatives synthesis.

ACKNOWLEDGMENTS

We wish to thank Maulana Azad College for providing necessary facility for research work.

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