



Trade Science Inc.

# Organic CHEMISTRY

*An Indian Journal**Full Paper*

OCAIJ, 7(4), 2011 [270-274]

## An efficient synthesis of 2-phenylimidazo [4, 5-f][1, 10] phenanthroline derivatives catalysed by boric acid under solvent free conditions at room temperature

Syed Shahed Ali

Department of Chemistry, Sir Sayyed College, Dr. Babasaheb Ambedkar Marathwada University,  
Aurangabad 431001, (INDIA)

E-mail: shahedali444@gmail.com

Received: 11<sup>th</sup> October, 2010 ; Accepted: 21<sup>st</sup> October, 2010**ABSTRACT**

Boric acid ( $\text{BO}_3\text{H}_3$ ) catalyzed three component improved procedure for the synthesis of various 2-Phenylimidazo [4, 5-f] [1, 10] phenanthrolines from 1, 10- phenanthroline-5, 6-dione, aromatic aldehydes and ammonium acetate at room temperature in excellent isolated yield has been reported. This is a simple and straight forward, high yielding, does not involve any hazardous or expensive catalyst. The synthesis is purely solvent free.

© 2011 Trade Science Inc. - INDIA

**KEYWORDS**

Boric acid;  
2-Phenylimidazo [4, 5-f]  
[1,10] phenanthrolines;  
Aromatic aldehyde;  
Boric acid;  
Ammonium acetate.

**INTRODUCTION**

Imidazoles are heterocycles with a wide range of applications and are receiving growing attention<sup>[1]</sup>. The imidazole ring system is of particular interest because it is a component of histidine and its decarboxylation metabolite histamine<sup>[2]</sup>. 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<sup>[3]</sup> (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<sup>[4]</sup>. In addition, the substituted imidazole ring systems are substantially used in ionic liquids<sup>[5]</sup> 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<sup>[6,7]</sup>. Also Siddiqui et al. proposed the synthesis of the imidazole using ionic liquids<sup>[8]</sup>. Recently, there are several methods reported in the literature for the synthesis of imidazoles using Zeolite HY/silica gel<sup>[9]</sup>,  $\text{ZrCl}_4$ <sup>[10]</sup>,  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ <sup>[11]</sup>, iodine<sup>[12]</sup>, sodium bisulfite<sup>[13]</sup>, acetic acid<sup>[14]</sup>. However these methods require prolonged reaction time and exotic reaction condition. Thus, the development of a new method for the synthesis of 2-Phenylimidazo [4, 5-f] [1, 10] phenanthrolines derivatives would be highly desirable. In recent years, boric acid ( $\text{BO}_3\text{H}_3$  or  $\text{B}[\text{OH}]_3$ ) have gained special attention as a catalyst in organic synthesis because many advantages such as excellent solubility in water, uncomplicated handling, inexpensiveness, eco-friendly nature. Readily, several synthetically useful organic transformations using boric acid as a catalyst have been reported in the literature<sup>[15]</sup>.

## EXPERIMENTAL

All chemicals were purchased from Merck, Aldrich and Rankem chemical companies and used without further purification. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. The progresses of the reactions were monitored by TLC (Thin Layer Chromatography). IR spectra were recorded on Perkin-Elmer FT spectrophotometer in KBr disc.  $^1\text{H}$  NMR spectra were recorded on an 300 MHz and 90MHz FT-NMR spectrometer in  $\text{CDCl}_3$  and DMSO as a solvent and chemical shift values are recorded in units  $\delta$  (ppm) relative to tetramethylsilane ( $\text{Me}_4\text{Si}$ ) as an internal standard.

## 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), boric acid (15 mol %) were ground together in a mortar with a pestle at room temperature for appropriate time 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,  $^1\text{H}$  NMR, mass, elemental analysis and melting points.

**1,10-Phenanthroline-5,6-dione:** Yellow solid mp. 260  $^\circ\text{C}$ ; Yield 40% (4.6 g);  $^1\text{H}$  NMR (300MHz, DMSO- $d_6$ ):  $\delta_{\text{H}}$  7.58-7.62(dd, 2H), 8.49-852 (dd, 2H), 9.11-9.13 (dd, 2H); GC-MS:  $m/z = 211$  ( $\text{M}^+$ ); Anal. Calcd for  $(\text{C}_{12}\text{H}_6\text{N}_2\text{O}_2)_3(\text{H}_2\text{O})$ : C, 66.67; H, 3.11; N, 12.96%. Found: C, 67.22; H, 2.97; N, 12.99%.

**2-phenyl-1H-imidazo[4,5-f][1,10]phenanthroline (3a):** Pale yellow solid; mp. 308  $^\circ\text{C}$ ,  $^1\text{H}$  NMR (90MHz,  $\text{CDCl}_3$ , DMSO- $d_6$ ):  $\delta_{\text{H}}$  13.48, (br., 1H), 9.04, (dd, 2H), 8.90, (d, 2H), 8.31, (d, 2H), 7.70, (dd, 2H), 7.49, (dd, 2H); LS-MS:  $m/z = 297$  ( $\text{M}^+$ ).

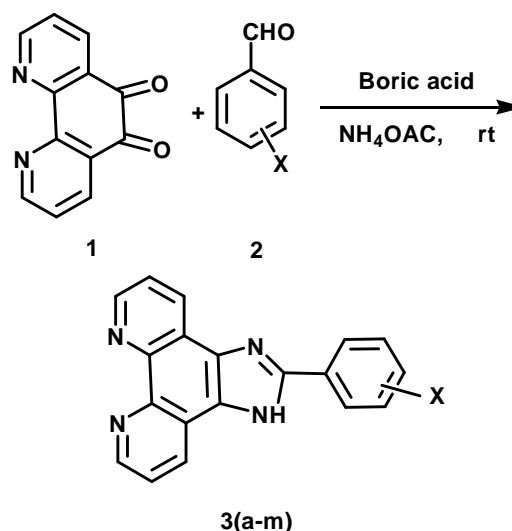
**2-(4-chlorophenyl)-1H-imidazo[4,5-f][1,10]phenanthroline (3b):** Pale yellow solid; mp. 307-308  $^\circ\text{C}$ ,  $^1\text{H}$  NMR (90MHz,  $\text{CDCl}_3$ , DMSO- $d_6$ ):  $\delta_{\text{H}}$  13.49, (br.s, 1H), 9.06, (dd, 2H), 8.92, (d, 2H), 8.27, (d, 2H), 7.72, (dd, 2H), 7.53, (d, 2H); GC-MS:  $m/z = 332$  ( $\text{M}^+$ ).

**4-(1H-imidazo[4,5-f][1,10] phenanthrolin-2-yl)Phenol (3c):** Pale yellow solid; mp. 300  $^\circ\text{C}$ , IR (KBr,  $\text{cm}^{-1}$ ): 3392 (stretch OH);  $^1\text{H}$  NMR (90MHz,  $\text{CDCl}_3$ , DMSO- $d_6$ ):  $\delta_{\text{H}}$  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:  $m/z = 313$  ( $\text{M}^+$ ); 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,  $\text{cm}^{-1}$ ): 3397, 3108, 1606, 1541, 1384, 1198, 739;  $^1\text{H}$  NMR (90MHz,  $\text{CDCl}_3$ , DMSO- $d_6$ ):  $\delta_{\text{H}}$  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:  $m/z = 342$  ( $\text{M}^+$ ).

## RESULTS AND DISCUSSION

As a part of our ongoing investigation in developing a versatile and efficient method for synthesis of heterocycles compounds<sup>[16,19]</sup> 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 boric acid (Scheme 1).

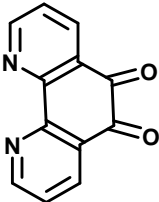
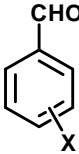
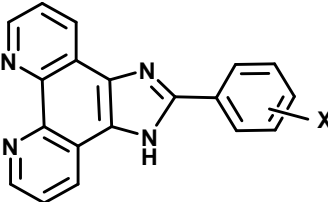
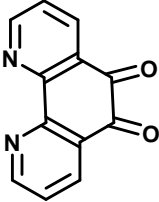
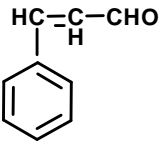
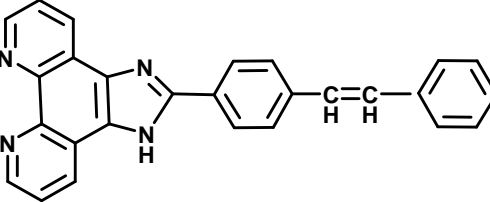
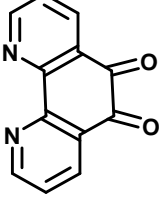
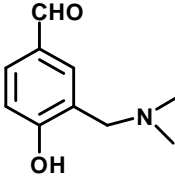
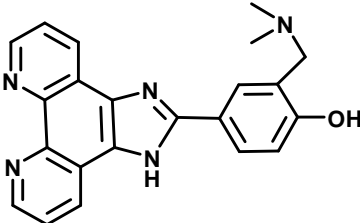
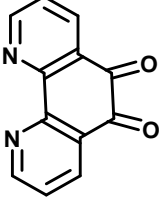
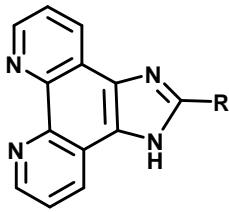


Scheme 1: Synthesis of 2-Phenylimidazo [4, 5-f] [1, 10] phenanthroline 3(a-m)

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 boric acid under solvent free condition. The mixture was ground to gather in a mortar with a

## Full Paper

TABLE 1: Synthesis of 2-Phenylimidazo [4, 5-f] [1, 10] phenanthroline using Boric acid catalyst under solvent free condition at room temperature.

Entry	Ketones (1)	Aldehydes (2)	Products 3(a-m)	Yield <sup>a,b</sup> (%)
1				
		a. X- H		96
		b. X- 4-Cl		96
		c. X- 4-OH		91
		d. X- 4-NO <sub>2</sub>		94
		e. X- 2-OH		93
		f. X- 3-NO <sub>2</sub>		89
		g. X- 2-NO <sub>2</sub>		95
		h. X- 4-CN		94
		i. X- 4-OMe		91
		j. X- 2,4,6-OMe		90
		k. X- 4-NMe <sub>2</sub>		94
2				90
3				90
4		R-CHO		
		l.R- CH <sub>3</sub> CHO		00
		m.R-CH <sub>3</sub> COCH <sub>3</sub>		00

<sup>a</sup>Yield of isolated pure products.<sup>b</sup>Products were characterized by IR, NMR, Mass elemental analysis and comparison with authentic sample.

pestle at room temperature for short reaction time, and then purified by column chromatography, substituted 2-Phenylimidazo [4, 5-f] [1, 10] phenanthrolines 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 boric acid were used. However no product formation was observed in absence of boric acid. By getting this result, we have extended this protocol to a variety of al-

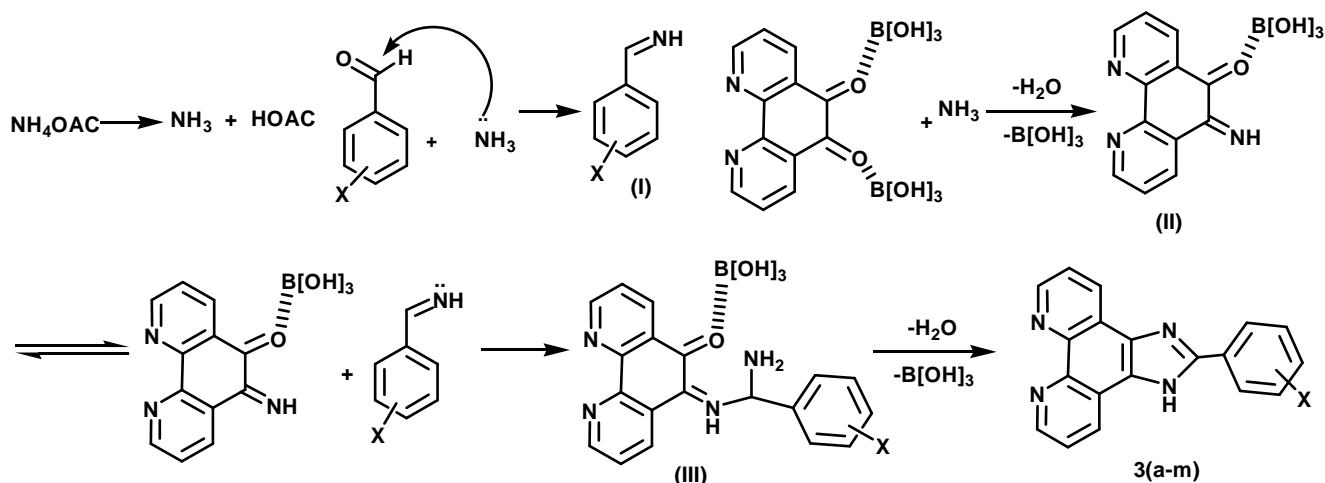
aldehydes and ketones summarized in TABLE 1. This protocol is rapid and efficient for the preparation of several substituted imidazoles from both electron efficient as well as electron deficient aromatic aldehydes. There is no effect on electron-withdrawing group and electron-donating group on reaction 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 imidzoles. 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 1). The boric acid increase the electrophilic character of aldehyde towards the ammonia to give the imines as intermediate I. Further imine I react with acetyl carbonyl to give intermediate III which on further dehydration afford the corresponding desired products (Scheme 2).

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

Entry	Time (min)	Yield (%)*	Boric acid (mol %)
1	20	00	No
2	10	traces	01
3	05	20	02
4	02	85	05
5	01	96	10
6	01	96	15

\*Isolated yield after column chromatography.



Scheme 2: Synthesis of 2-phenylimidazo [4, 5-f] [1, 10] phenanthroline

In conclusion, the boric acid 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.

#### ACKNOWLEDGEMENTS

We wish to thank *Md. Tilawat Ali* the president of

Sir Sayyed College for providing necessary facility for research work.

#### REFERENCES

- [1] (a) J.G.Lambardino, E.H.Wiseman; *J.Med.Chem.*, **17**, 118-1188 (1974); (b) A.P.Philips, H.L.White, S.Rosen; *Eur.Pat.Appl.*, ED 58890 (1982).
- [2] C.R.Ganellin, In 'Medicinal Chemistry in Drug Research'; S.M.Roberts, J.B.Price (Eds); Academic press: New York, 93-119 (1985).
- [3] (a) D.T.Hill, G.R.Girard, J.Wrinstock, R.M.Edwards, E.F.Wridles, E.Ohlstain, C.E.Peishoff, E.Baker, N.Aiyar; *Bioorg.Med.Chem.Lett.*, **5**, 19 (1995);

## Full Paper

- (b) D.B.Judd, M.D.Dowle, D.Middlemiss, D.I.Scopper, B.C.Ross, I.T.Jack, M.Pass, E.Tranquillini, J.E.Hobson, T.A.Panchal, P.G.Stuart, J.M.S.Parton, J.Hubbard, A.Hildiicth, G.M.Drew, J.M.Roberston, L.K.Clark, A.Jraves, A.A.E.Hunt, J.Polley, P.J.Eddershaw, M.K.Bayliss, G.R.Manchee, M.D.Donnely, D.G.Walker, S.A.Richards; *J.Med.Chem.*, **37**, 3108 (1994); (c) S.K.Thompson, K.H.M.Murthy, B.Zhao, E.Winborne, D.W.Green, S.M.Fisher, R.L.Desjarlais, T.A.Tomaszek, J.D.Meck, J.G.Glwnson, S.S.Abdel-Meguid; *J.Med.chem.*, **37**, 3100 (1994); (d) D.M.Rotstein, D.J.Kertesz, K.A.M.Walder, D.C.Swinny; *J.Med.Chem.*, **35**, 2818 (1992); (e) R.N.Brodgen, T.M.Heel, G.S.Avery; *Drugs*, **15**, 93 (1978).
- [4] S.S.Abdel-Meguid, B.W.Meteall, T.J.Corr. P.Demarsh, R.L.Desjarlais, S.Fisher, D.W.Green, L.Ivanoff, D.M.Lambert, K.H.M.Murthy, S.R.Petteway, W.J.Pitts Jr., T.A.Tomaskzek, E.Winborn Jr., B.Zhao, G.B.Dreyer, T.D.Meek; *Biochemistry*, **33**, 11671 (1994).
- [5] P.Wasserscheid, W.Keim; *Angew.Chem.Int.Ed. Eng.*, **39**, 37872 (2000).
- [6] D.Bourissou, O.Guerret, F.T.Ggabai, G.Bertrand; *Chem.Rev.*, 100 (2000).
- [7] B.Radziszewski; *Chem.Ber.*, **15**, 1493(1882).
- [8] F.R.Japp, H.H.Robinson; *Chem.Bar.*, **15**, 1268 (1882).
- [9] (a) S.A.Siddiqui, K.V.Srinivasan; *Synthesis*, **17**, 2849 (2006); (b) J.L.D.Wang Jr., R.Mason, P.Amoyaw Jr., X.R.Bu; *J.Org.Chem.*, **70**, 2353-2356 (2005).
- [10] S.Balalaie, A.Arabanian, M.S.Hashtroudi; *Mont. Fur.Chem.*, **131**, 945 (2000).
- [11] G.V.M.Sharma, Y.Jyothi, P.S.Lakshmi; *Syn.Comm.*, **36**, 2991 (2006).
- [12] M.M.Heravi, K.Bakhtiari, H.A.Oskooie, S.Taheri; *J.Mol.Catal.A:Chem.*, **263**, 279 (2007).
- [13] M.Kidwai, P.Mohtsra, V.Bansal, R.Goyal; *Mont.Fur. Chem.*, **137**, 1189 (2006).
- [14] J.N.Sangshetti, N.D.Kokare, S.A.Kothakar, D.B.Shinde; *Mont.Fur.Chem.*, **139**, 125 (2008).
- [15] S.E.Wolkenberg, D.D.Winoski, W.H.Leister, Y.Wang, Z.Zhao, C.W.Lindsley; *Org.Lett.*, **6**, 1453 (2004).
- [16] (a) S.J.Tu, X.T.Zhu, F.Fang, X.J.Zhang, S.L.Zhu, T.J.Li, D.Q.Shi, X.S.Wang, S.J.Ji; *Tetrahedron Lett.*, **44**, 6153 (2003); (b) T.Pingwah; *Org.Synt.*, **81**, 262 (2005); (c) M.K.Chaudhuri, S.Hussain, M.Lakshmi Kantam, B.Neelima; *Tetrahedron Lett.*, **46**, 8329 (2005); (d) S.J.Tu, X.T.Zhu, X.J.Fang Zuang, S.L.Zhu, T.J.Li, D.Q.Shi, X.S.Wang, S.J.Ji; *Chine. J.Chem.*, **23**, 596 (2005); (e) M.K.Chaudhuri, S.Hussain; *J.Mol.Cat.*, **A269**, 214 (2007); (f) V.M.Gurav, K.G.Huge, R.Bandichhor, P.Pratap Reddy, A.Bhattacharya, R.Vijaya Ananda; *Tetrahedron Lett.*, **49**, 106 (2008); (g) A.Kumar, R.A.Maurya; *Tetrahedron Lett.*, **49**, 5471 (2008).
- [17] R.V.Hangarge, B.K.Karale, A.S.Mane, V.P.Chavan, D.V.Jarikote, M.S.Shingare; *Green Chem.*, **3**, 310 (2001).
- [18] S.S.Shindalkar, B.R.Madje, M.S.Shingare; *J.Korean Chem.Soc.*, **49**, 377 (2005).
- [19] S.S.Shindalkar, B.R.Madje, R.V.Hangarge, M.S.Shingare; *Ind.Chem.*, **44B**, 2409 (2005).
- [20] (a) S.S.Shindalkar, B.R.Madje, M.S.Shingare; *Ind.J.Hetero.Chem.*, **15**, 81 (2005); (b) K.F.Shelke, B.R.Madje, S.A.Sadaphal, N.V.Shitole, M.S.Shingare; *Org.Chem.: Ind.J.*, **4**, 277 (2008).