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An Efficient Synthesis of 2,4,5-Triaryl-1*H*-Imidazole Derivatives Catalyzed by Boric Acid IN Green Condition

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Abstract: *Boricacid (BO3H3) is an inexpensive, efficient and mild catalyst for the synthesis of 2,4,5-triaryl-1H-imidazoles in excellent yields from the one-pot three-component condensation of benzil/ benzoin, an aldehydes and ammonium acetatein aqueous media under ultrasound at room temperature. The remarkable advantages offered by this method are green catalyst, mild reaction conditions, simple procedures, much faster reactions and excellent yield of products.*

Keywords: 2,4,5-Triaryl-1*H*-imidazole, Boric acid, Aqueous media, Ultrasound irradiation

I. INTRODUCTION

2,4,5-Triaryl-1H-imidazole compounds have gained the remarkable importance due to their widespread biological activities and their use in synthetic chemistry. Imidazole ring system is one of the most important substructure found in a large number of natural products and pharmacologically active compounds such as ant ulcerative agent cimetidine,1 the proton pump inhibitor omeprazole2and the benzodiazepine antagonist flumazenil 3 are imidazole derivatives. Trifenagrel 4 is a 2,4,5-triaryl-1H-imidazole that reduces platelet aggregatetion in several animal species and humans.[1-6]

Due to their great importance, many synthetic strategies havebeendeveloped.In1882,RadziszewskiandJapp reported thefirstsynthesisoftheimidazolefrom1,2-dicarbonylcom- pound, various aldehydes and ammonia, to obtain the 2,4,5-tripheny limidazoles.[7-8] Also, Grimmettet al. proposed the synthesis of the imidazole using nitrile sandesters.[9] Recently, there are several methods reported in the literature for the synthesisof2,4,5-triaryl-1H-imidazolesfrombenzil/benzoin, aldehydes and ammonium acetate using different catalyst such as zeolite HY/silica gel, 8ZrCl4, 9NiCl2.6H2O, [10]ionicliquid, [11][12]iodine, [1415]sodiumbisulfite, [16]acidicAl_2O_3, [18]AcOH, [19]NH4OAc, [20]Yb(OTf)3. [21]However, these methods require prolonged reaction time and exotic reaction condition. Thus, the development of a new method for the synthesis of 2,4,5- triaryl-1H-imidazoles derivatives would be highly desirable.[23-30]

In 1980, Breslow discovered that the Diels-Alder reaction performed in water could be subjected to huge rate accelerations. [31-33] To date, many more organic transformations have been carried out in water or aqueous media. [34] In recent years, boric acid (BO3H3orB[OH]3) have gained special attention as catalyst in organic synthesis because many advantages such as excellent solubility in water, uncomplicated handling, inexpensiveness and eco-friendly nature. Recently, several synthetically useful organic transformations using boric acid as a catalyst have been reported in the literature. [35-44] Ultrasound has increasingly been used in organic synthesis in the last three decades. [45-49] It has been demonstrated as an alternative energy source for organic reactions ordinarily accomplished by heating. A large number of organic reactions can be carried out in higher yields, shorter reaction time or milder conditions under ultrasound irradiation.[50-60]

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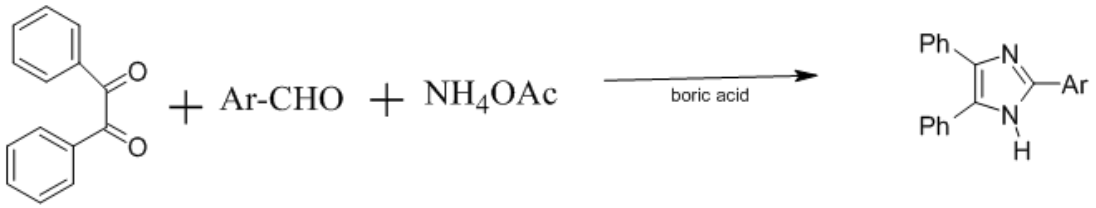
II. EXPERIMENTAL

The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. IR spectra were recorded on Perkin-ElmerFT spectrophotometer in KBr disc.[1] H NMR spectra were recorded on an 80 MHz FT-NMR spectrometer in CDCl3 as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard. Bandelin Sonorex (35 kHz) ultrasonic bath was used for ultrasonic irradiation. Mass spectra were recorded on Micro mass Quattro II using electro spray Ionization technique.

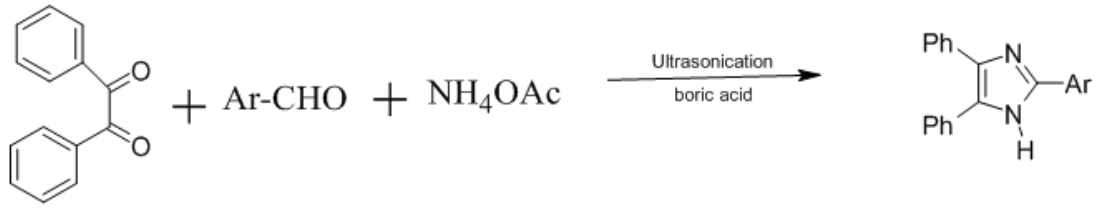
General procedure for the synthesis of 2,4,5-triary-1*H*- Imidazole(3a-l). BO_3H_3 (5 mol%) benzil**1**/benzoin **4** (1 mmol), and ammonium acetate (3 mmol) dissolved in water- ethanol(5:5mL)were taken in single neck round bottom flask and to this aldehyde (1 mmol) was added. The flask with the reaction mixture was immersed into the water bath of an ultrasoniccleaneratroomtemperatureforthepresc ribedtime(Table2).Theprogressofthereactionwasmonitoredon TLC (petroleum ether: ethylacetate=9:1aseluent).Then reaction mixture was poured on ice-water (50 mL), and precipitated solid was filtered, washed with water, dried and recrystallize from ethanol to get the corresponding 2,4,5-triaryl-1*H*-imidazoles(**3a-l**). The products (**3a-l**) were confirmed by comparisons with authentic samples, IR, ^{1}H NMR, mass spectra and melting points.

2.1 Reaction Scheme

Reaction 1



Reaction 2



III. RESULT AND DISCUSSION

As a part of our ongoing investigation in developing a versatile and efficient method for synthesis of heterocyclic compounds,[19,21d,e,22] we report here an efficient synthetic method for the synthesis of 2,4,5-triarylimidazoles from benzil/benzoin, aldehydes and ammonium acetate in the presence of boric acid (Scheme 1, 2).We initially studied the catalytic efficiency of boric acid for (Table 2, compound **3b**), we first examined the reaction without ultrasound at room temperature. We found low yield (40%) with prolonged reaction time (180 min) and using ultrasound room temperature amazingly we found excellent the synthesis of2-(2-chlorophenyl-4,5-diphenyl-1*H*-imidazole(Table 2, compound **3b**) using benzil/benzoin**,** 2-chlorobenz- aldehyde and ammonium acetate in different solvents and various mol% of boric acid (Table 1). From Table 1, the reactions in pure water and ethanol afforded 2-(2-chloro- phenyl)-4,5-diphenyl-1*H*-imidazole in low yields after 160 and 180 min, respectively (Table 1, entry 1, 2). The use of THF and CH_3CN as co solvent delivers low yields (Table 1, entry3,4)as compared to optimized reaction condition(Table 1, entry 6). A quantitative yield of desired product was obtainedinthepresenceof5mol%boricacidfor40/70min; indicating that the boric acid (5 mol%) H2O/EtOH (5:5 mL) catalytic system is highly active for this reaction. Even we changed the ratio of water and ethanol, but we observed that

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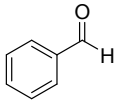
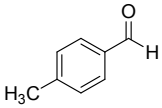
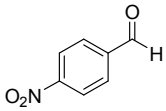
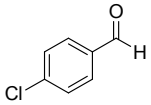
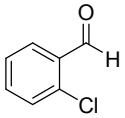
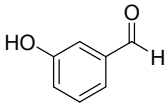
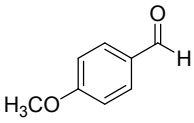
Table 1: Optimization of reaction condition and mol% of boric acid using benzil, 2-chlorobenzaldehyde and ammonium acetate under ultrasonication at room temperature (Table 2, compound **3b**)

	Solvent	(mol%)	Yield(%)[a]	Yield (%)[a]
1	pure H2O(10)	10	90/70	120/65
2	pure EtOH(10)	10	90/66	110/60
3	H2O/THF(5:5)	10	60/87	90/80
4	H2O/CH3CN(5:5)	10	80/82	100/76
5	H2O/EtOH(5:5)	10	35/98	60/94
6	H2O/EtOH(5:5)	5	40/98	70/94
7	H2O/EtOH(5:5)	2.5	60/87	90/84
8	H2O/EtOH(2:8)	5	60/76	100/67
9	H2O/EtOH(3:7)	5	50/80	90/72

Table 2

Entry	Aldehyde	Time (min)	Yield (%)	M. P. °C	
				Found	Lit[19]
3a		2	86	220-222	218-222
3b		3	84	197-198	195-198
3c		6	78	162-166	160-163
3d		7	92	160-164	158-161
3e		6.5	83	150-154	152-155
3f		5.5	89	92-96	95-97
3g		5	80	188-192	184-187

IV. CONCLUSION

In conclusion, we have developed an ultrasound-assisted, efficient and convenient method for the one-pot three component synthesis of 2,4,5-triarylimidazole derivatives using cheap and readily available boric acid as a catalyst. Then table merits offered by this methodology are mild reaction conditions, simple procedures, cleaner reactions, short reaction times and excellent yields of products.

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REFERENCES

[1]. J.J. Li, Ed. Heterocyclic Chemistry in Drug Discovery, John Wiley &Sons: Hoboken, **2013**. [Google Scholar], [Publisher]

[2]. D.D. Patil, D.K. Mhaske, G.C. Wadhawa, *J. Adv. Pharm. Educ. Res.*, 2011, *2*, 104-112. [Google Scholar], [Publisher]

[3]. W.A. Denny, G.W. Rewcastle, B.C. Baguley, *J. Med. Chem.*, **1990**, *33*, 814–819. [Crossref], [Google Scholar], [Publisher]

[4]. N.A. Mirgane, V.S. Shivankar, S.B. Kotwal, G.C. Wadhawa, M.C. Sonawale, *Mater. Today: Proceedings*, **2021**, *37*, 849-853. [Crossref], [Google Scholar], [Publisher]

[5]. S.S. Nayak, N.A. Mirgane, V.S. Shivankar, K.B. Pathade, G.C. Wadhawa, *Mater. Today: Proc.*, **2021**, *37*, 2302-2305. [Crossref], [Google Scholar], [Publisher]

[6]. N.A. Mirgane, V.S. Shivankar, S.B. Kotwal, G.C. Wadhawa, M.C. Sonawale, *Mater. Today: Proc.*, **2021**, *37*, 886-889. [Crossref], [Google Scholar], [Publisher]

[7]. N.A. Mirgane, A. Chandore, V. Shivankar, Y. Gaikwad, G.C. Wadhawa, *Res. J. Pharm. Technol.*, **2021**, *14*, 2686-2690. [Crossref], [Google Scholar], [Publisher]

[8]. S.S. Nayak, N.A. Mirgane, K.B. Pathade, V.S. Shivankar, G.C Wadhawa, *Plant Sci. Today*, **2021**, *8*, 425-428. [Crossref], [Google Scholar], [Publisher]

[9]. A.K. Valvi, S.S. Nayak, V.S. Shivankar, G.C. Wadhawa, *Mater. Today: Proc.*, **2021**. [Crossref], [Google Scholar], [Publisher]

[10]. D. Davey, P.W. Erhadt, W.C. Lumma Jr., J. Wiggins, M. Sullivan, D. Pang, E. Cantor, *J. Med. Chem.,* **1987**, *30*, 1337–1342. [Crossref], [Google Scholar], [Publisher]

[11]. B.E. Tomczuk, C.R. Taylor Jr., L.M. Moses, D.B. Sutherland, Y.S. Lo, D.N., Johnson, W.B. Kinnier, B.F. Kilpatrick, *J. Med. Chem.*, **1991**, *34*, 2993–3006. [Crossref], [Google Scholar], [Publisher]

[12]. A.A. Spasov, I.N. Yozhitsa, L.I. Bugaeva, V.A. Anisimova, *Pharm. Chem. J.*, **1999**, *33*, 232–243. [Crossref], [Google Scholar], [Publisher]

[13]. S.S. Nayak, G.C. Wadhawa, V.S. Shivankar, D.D. Patil, M.C. Sonawale, N.A. Mirgane, *Mater. Today: Proc.*, **2021**, *37*, 2490-2494. [Crossref], [Google Scholar], [Publisher]

[14]. M. Shaharyar, A. Mazumder, M.J. Ahsan, *Arabian J. Chem.*, **2014**, 7, 418–424. [Crossref], [Google Scholar], [Publisher]

[15]. D.K. Mhaske, D.D. Patil, G.C. Wadhawa, *Int J Pharm Biomed Res*, **2011**, *2*, 107-11. [Google Scholar], [Publisher]

[16]. D. Kumar, D.N. Kommi, R. Chebolu, S.K. Garg, R. Kumar, A.K.Chakraborti, *RSC Adv.*, **2013**, *3*, 91–98. [Crossref], [Google Scholar], [Publisher]

[17]. S.B. Rathod, M.K. Lande, B.R. Arbad, *Bull. Korean Chem. Soc.*, **2010**, *31*, 2835-2840. [Crossref], [Google Scholar], [Publisher]

[18]. S.S. Nayak, N.A. Mirgane, V.S. Shivankar, K.B. Pathade, G.C. Wadhawa, *Mater. Today: Proc.*, **2021**, *37*, 2427-2431. [Crossref], [Google Scholar], [Publisher]

[19]. P.S. Gaikar, V.S. Shivankar, P.A. Patil, A.U. Chavan, G.C. Wadhawa, *Int. J. Aquatic Sci.*, **2021**, *12*, 4973-4980. [Google Scholar], [Publisher]

[20]. E. Mentese, H. Bektaş, S. Ülker, O. Bekircan, B. Kahveci, *J. Enzyme Inhib. Med. Chem.*, **2014**, *29*, 64–68. [Crossref], [Google Scholar], [Publisher]

[21]. D. Secci, A. Bolasco, M. D'Ascenzio, F. dellaSala, M. Yáñez, S. Carradori, *J. Heterocyclic Chem.*, **2012**, *49*, 1187. [Crossref], [Publisher]

[22]. J.P. Tripathi, V.K. Kasana, *Int. J. Res. Appl. Sci. Eng. Tech.*, **2018**, *6,* 64-68. [Google Scholar], [Publisher]

[23]. S.S. Nayak, G.C. Wadhawa, K.B. Pathade, V.S. Shivankar, N.A. Mirgane, *Plant Science Today*, **2021**, *8*, 380-385. [Crossref], [Google Scholar], [Publisher]

[24]. A. Rao, A. Chimirri, S. Ferro, A.M. Monforte, P. Monforte, M. Zappalà, *ARKIVOC*, **2004**, *5*, 147-155. [Crossref], [Google Scholar], [Publisher]

IJARSCT
ISSN (Online) 2581-9429
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[25]. G.C. Wadhawa, V.S. Shivankar, S.S. Patil, Y.A. Gaikwad, A.V. Satere, B. Rode, C.H. Gill, L.V. Gavali, *Rasayan J. Chem.*, **2017**, *10*, 3-15. [Google Scholar], [Publisher]

[26]. H.T.B. Bui, Q.T.K. Ha, W.K. Oh, D.D. Vo, Y.N. Chau, C.T. Tu, E.C. Pham, P.T. Tran, L.T. Tran, Van Mai H., *Tetrahedron Lett.*, **2016**, *57*, 887–891. [Crossref], [Google Scholar], [Publisher]

[27]. J.S. Yadav, Y.K. Srivastava, *Rasayan J. Chem.*, **2010**, *3*, 726-730. [Google Scholar], [Publisher]

[28]. D.D. Rishipathak, S.C. PAL, **2007**, *19*, 3242-3244. [Google Scholar], [Publisher]

[29]. D.D. Patil, D.K. Mhaske, G.C. Wadhawa, *Int. J. Pharm. Sci. Res.*, **2011**, *2*, 2750-2752. [Google Scholar], [Publisher]

[30]. R. Javahershenas, J. Khalafy, R. Herman Prager, *J. Chem. Rev.*, **2019**, *1*, 233-242. [Crossref], [Google Scholar], [Publisher]

[31]. B. Kahveci, N. Sosan, E. Mentese, F. Yilmaz, *Rev. Roum. Chim.*, **2013**, *58*, 511-515. [Google Scholar], [Publisher]

[32]. D.D. Patil, D.K. Mhaske, G.C. Wadhawa, *Int. J. Pharm. Sci. Res.*, **2011**, *2*, 1464-1466. [Crossref], [Google Scholar], [Publisher]

[33]. G. Navarrete-Va´zquez*et,* H. Moreno-Diaz, S. Estrada-Soto, M. Torres-Piedra, I. León-Rivera, H. Tlahuext, O. Muñoz-Muñiz, H. Torres-Gómez*, Synth. Commun.*, **2007**, *37*, 2815–2825. [Crossref], [Google Scholar], [Publisher]

[34]. C.H. Gill, G.C. Wadhawa, L. Gavali, V.S. Shivankar, K. Pawar, *Res. J. Pharm. Pharm.,* **2018**, *10*, 103-104. [Crossref], [Google Scholar], [Publisher]

[35]. A.T. Khan, T. Parvin, L.H. Choudhury, *Synth. Commun*., **2009**, *39*, 2339–2346. [Crossref], [Google Scholar], [Publisher]

[36]. G.C. Wadhawa, V.S. Shivankar, Y.A.G. Charansingh, H. Gill, L.V. Gavali, *World J. Pharm. Res.,* **2018**, *7*, 483-495. [Google Scholar], [Publisher]

[37]. Z. Li, H. Huang, H. Sun, H. Jiang, H. Liu, *J. Comb. Chem.*, **2008**, *10,* 484-486. [Crossref], [Google Scholar], [Publisher]

[38]. A. Saberi, *Iran. J. Sci. Technol.*, **2015**, *39*, 7-10. [Crossref], [Google Scholar], [Publisher]

[39]. A. Valvi, G.C. Wadhawa, S.S. Nayak, V.S. Shivankar, *Int. J. Aquat. Science*, **2021**, *12*, 4769-4775. [Google Scholar], [Publisher]

[40]. H. Naeimi, Z. babaei, *Green Chem. Lett. Rev.*, **2017**, *10*, 129–133. [Crossref], [Google Scholar], [Publisher]

[41]. G.C.Wadhawa, V.S. Shivankar, D.D. Patil, Y.A. Gaikwad, L.V. Gavali, C.H. Gill, *World J. Pharm. Pharm. Sci.* **2016**, *5*, 624-656. [Crossref], [Google Scholar], [Publisher]

[42]. G.S. Getvoldsen, N. Elander, A.A. Stone-Elander, *Chem. Eur. J.*, **2002**, *8*, 2255-2260. [Crossref], [Google Scholar], [Publisher]

[43]. N. Boufatah, A. Gellis, J. Maldonado, P. Vanelle, *Tetrahedron*, **2004**, *60*, 9131-9137. [Crossref], [Google Scholar], [Publisher]

[44]. S. Sajjadifar, H. Hamidi, K. Pal, *J. Chem. Rev.*, **2019**, *1*, 35-46. [Crossref], [Google Scholar], [Publisher]

[45]. R. Martinez-Palou, L.G. Zepeda, H. Höpfl, A. Montoya, D.J. Guzman-Lucero, J. Guzman, *Mol Divers.,* **2005**, *9*, 361-369. [Crossref], [Google Scholar], [Publisher]

[46]. G.C. Wadhawa, V.S. Shivankar, D.D. Patil, Y.A. Gaikwad, L.V. Gavali Gill , C.H., *World J. Pharm. Pharm. Sci.*, **2016**, *5*, 624-656. [Google Scholar], [Publisher]

[47]. S.Y. Lin, Y. Isome, E. Stewart, J.F. Liu, D. Yohannes, L. Yu, *Tetrahedron Lett.*, **2006**, *47*, 2883-2886. [Crossref], [Google Scholar], [Publisher]

[48]. A. Belgasem Mezoughi, W. Abdussalam Mohammed, Z. O. Ettarhouni, *J. Chem. Rev.*, **2021**, *3*, 196-218. [Crossref], [Google Scholar], [Publisher]

[49]. O. Algul, A. Kaessler, Y. Apcin, A. Yılmaz, J. Jose, *Molecules*, **2008**, *13*, 736-748. [Crossref], [Google Scholar], [Publisher]

[50]. K.M. Hosamani, H.R. Seetharamareddy, R.S. Keri, M.S. Hanamanthagouda, M.G. Moloney, *J. Enzyme Inhib. Med. Chem.*, **2009**, *24*, 1095-1100. [Crossref], [Google Scholar], [Publisher]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
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Impact Factor: 6.252

[51]. S. Asirvatham; E. Thakor; H. Jain, *J. Chem. Rev.*, **2021**, *3*, 247-272. [Crossref], [Publisher]
[52]. A. Ben-Alloum, S. Bakkas, M. Soufiaoui, *Tetrahedron Lett.*, **1998**, *39*, 4481-4484. [Crossref], [Google Scholar], [Publisher]
[53]. M.A.H. Zahran, F.A.A. El-Essawy, S.M. Yassin, T.A.R. Salem, N.M. Boshta, *Archive der Pharmzie.*, **2007**, *340*, 591-598. [Crossref], [Google Scholar], [Publisher]
[54]. D.D. Patil, G.C. Wadhawa, A.K. Deshmukh, K.B. Pathade, P.B. Shinde, P.B. Chordiya, A.S. Kulal, **2010**. [Google Scholar]
[55]. X. Wen, J. El Bakali, R. Deprez-Poulain, B. Deprez, *Tetrahedron Lett.*, **2012**, 53, 2440-2443. [Crossref], [Google Scholar], [Publisher]
[56]. G. Wadhawa, V.S. Shivankar, Y.A. Gaikwad, N.S. Dhumale, C.H. Gill, L.V. Gavali, *World J. Pharm. Pharm. Sci.*, **2017**, *7*, 1013-1019. [Google Scholar], [Publisher]
[57]. K. Niknam, A. Fatehi-Raviz, *Iran. Chem. Soc.*, **2007**, *4*, 438-443. [Crossref], [Google Scholar], [Publisher]
[58]. D. Rajiv, S.K. Sonwane, S.K. Srivastava, S.D. Srivastava, *Chem. Pharm. Res.*, **2010**, *2*, 415-423. [Google Scholar], [Publisher]
[59]. V.S. Devi, M.G. Rao, *World J. Pharm. Pharm. Sci.*, **2014**, *3*, 1516-1525. [Google Scholar], [Publisher]
[60]. Z.H. Zhang, L. Yin, Y.M. Wang, *Catal. Commun.*, **2007**, *8*, 1126-1131. [Crossref], [Google Scholar], [Publisher]