



Research Article

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## Catalyst free synthesis of imidazoles: Characterization and its antimicrobial activity

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### ABSTRACT

A series of tri substituted imidazoles were synthesized in good yields by one pot three component condensation of benzil, aldehyde and ammonium acetate. The notable features of this methodology are simple procedure, cost effective and product purified by non- chromatographic techniques. The as-synthesized derivatives are characterized by IR, NMR and Mass spectroscopy. From the spectroscopic results the proposed structure of the imidazole derivatives was predicted. Moreover, its antimicrobial activity is also tested by disc diffusion technique.

**Keywords:** Imidazoles, One pot condensation, Multi component reactions, Antimicrobial activity

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### INTRODUCTION

Heteroaromatic compounds containing imidazole nucleus play a vital role in many pharmaceutical and biochemical applications. In addition, highly substituted imidazoles are found to possess antibacterial, anti-inflammatory, antihypertensive, antithrombotic, antiviral, anti-allergic, analgesic, fungicidal, and herbicidal properties. Furthermore, it acts as ionic liquids for many organic reactions especially in organo-metallic catalysis [1-5]. Its contribution in photography as photosensitive material is significant. As it possess donor – acceptor  $\pi$  conjugation they offer many optoelectronic application such as Non Linear Optics (NLO), Dye Sensitized Solar Cells (DSSC), Organic Light Emitting Diodes (OLEDs) and molecular switches, etc., [6-8].

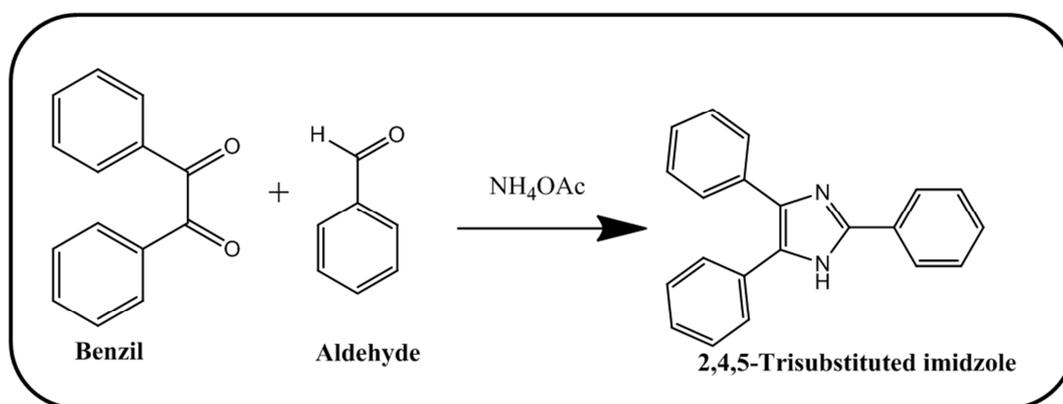
Owing to its wide range of application, many researchers are currently focused on the synthesis of tri and tetra substituted imidazole in good yield and easy synthetic procedure. Though there are number of divergent methods available in the literature, Radziszewski was the first one to report the synthesis of the imidazole in 1882 which comprises the condensation of 1, 2 dicarbonyl compounds, aldehyde and ammonium acetate. Though this method has lot of potential it was not suited for some variants. In order to reduce the complexity of the reaction and to improve the yields several research groups suggest various routes by modifying the solvents and catalyst such as acetic acid, SiO<sub>2</sub> supported H<sub>2</sub>SO<sub>4</sub>, InCl<sub>3</sub>.H<sub>2</sub>O, ZnO, amino acid, silica supported metal salts Al<sub>2</sub>O<sub>3</sub>, KH<sub>2</sub>PO<sub>4</sub> etc., [9-12] the above mentioned catalyst increases the yield, but separation of catalyst from the reaction mixture is a tedious process, likewise each synthesis has its own merits and demerits. Multi component reactions have drawn much interest holding an outstanding place in modern organic syntheses which allow the assembly of complex molecules in one pot and show a facile execution, high atom economy and high selectivity. In view of this, to overcome the above shortcomings, we have planned to synthesize the tri substituted imidazole derivatives under catalyst free, simple and environmentally benign route and the compound is purified by non-chromatographic techniques.

## EXPERIMENTAL SECTION

Benzil, Substituted aldehyde and Ammonium acetate from Merck, Solvents such as ethanol, methanol, diethyl ether and acetone are of analytical grade. All chemicals were used without further purification. Elemental analysis was carried out using Perkin-Elmer, 240 elemental analyser. IR spectra were recorded on a Perkin- Elmer FT-IR spectrometer in the range of 4000  $\text{cm}^{-1}$  to 400  $\text{cm}^{-1}$  using KBr pellets.  $^1\text{H}$  NMR spectra were recorded on a Bruker WP 300MHz using DMSO- $d_6$  as a solvent containing TMS as the internal standard.  $^{13}\text{C}$  NMR were recorded with Bruker DRX-400 spectrometer at 400 and 100MHz respectively. Mass Spectra were obtained by Thermoscientific LT2 X2 model ESI of  $m/z$  range 30-600, solvents used was DMSO (Aldrich). Antimicrobial susceptibility test is carried out using disc diffusion technique.

**Synthesis of tri substituted imidazole derivatives:**

A sample of benzil (1mM), substituted benzaldehyde(1mM) and ammonium acetate(4mM) in an ethanolic medium is taken in 50 ml round-bottom flask, and this mixture was refluxed for 6 h at 140°C. The progress of the reaction was monitored by TLC using Toluene :ethylacetate (7:3) eluent. The reaction mixture was cooled and washed three times with hot water. The solution was brought to dryness and then was washed with methanol and re crystallized using hot methanol. The solid was dried under vacuum to give a required product.



Scheme 1. Schematic representation of synthesis of tri substituted imidazoles

## RESULTS AND DISCUSSION

Aromatic aldehyde used for the present synthesis and the products obtained are listed in the Table 1.

Table 1. List of aldehyde used in the above scheme

S.No	Aldehyde	Name of the synthesized compound
1	Naphthalene aldehyde	2-(naphthalene-1-yl)-4,5-diphenyl-1H-imidazole (TPI-6)
2	Anthracene-9-carbaldehyde	2-(anthracen-9-yl)-4,5-diphenyl-1H-imidazole (TPI-7)
3	Pyrene-4-carbaldehyde	2-(3a',6-dihydroxyren-1-yl)-4,5-diphenyl-1H-imidazole (TPI-8)
4	4-(methylthio)benzaldehyde	2-(4-(methylthio)phenyl)-4,5-diphenyl-1H-imidazole (TPI-9)
5	3-Bromobenzaldehyde	2-(3-bromophenyl)-4,5-diphenyl-1H-imidazole (TPI-10)

**Compound TPI-6:**

Anal. Calcd. For  $\text{C}_{25}\text{H}_{18}\text{N}_2$ : C, 86.68; H, 5.24; N, 8.09 Found: C, 87.01; H, 5.30; N, 8.27; Yield (79%), ESI-MS 346.42(M+H);  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  7.5 ppm (Ar-H, multiplet),  $\delta$  12.8 ppm (Ar-NH, singlet),  $^{13}\text{C}$ -NMR:  $\delta$  147 ppm (C=N), IR KBr ( $\text{cm}^{-1}$ ): 1642(C=Nstr), 1521 (C=Cstr), 3432 (N-H str) 3089 (C-Hstr).

**Compound TPI-7:**

Anal. Calcd. For  $\text{C}_{29}\text{H}_{20}\text{N}_2$ : C, 87.85; H, 5.08; N, 7.78 Found: C, 87.83; H, 5.11; N, 7.83; Yield (81%), ESI-MS 396.48(M+H);  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  7.6 ppm (Ar-H, m),  $\delta$  12.5 ppm (Ar N-H, s),  $^{13}\text{C}$ -NMR:  $\delta$  149 ppm (C=N), IR KBr ( $\text{cm}^{-1}$ ): 1679(C=Nstr), 1518 (C=Cstr), 3244 (N-H str) 3041 (C-Hstr).

**Compound TPI-8:**

Anal. Calcd. For  $\text{C}_{31}\text{H}_{22}\text{N}_2$ : C, 88.12; H, 5.25; N, 6.63 Found: C, 88.19; H, 5.31; N, 6.69; Yield (77%), ESI-MS 422.52(M+H);  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  6.6 ppm (Ar-H, m),  $\delta$  11.8 ppm (Ar N-H, s),  $^{13}\text{C}$ -NMR:  $\delta$  158 ppm (C=N), IR KBr ( $\text{cm}^{-1}$ ): 1638(C=Nstr), 1526(C=Cstr), 3328 (N-H str) 3080 (C-Hstr).

**Compound TPI-9:**

Anal. Calcd. For C<sub>22</sub>H<sub>18</sub>N<sub>2</sub>S: C,77.16; H, 5.30; N, 8.18;S,9.36 Found: C, 77.19; H, 5.36; N, 8.25;S,9.43 Yield (87%),ESI-MS 342.12(M+H); <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ 7.4 ppm (Ar-H, m), δ 12.6 ppm (Ar N-H, s), <sup>13</sup>C-NMR: δ154 ppm (C=N), IR KBr (cm<sup>-1</sup>): 1678(C=Nstr), 1592 (C=Cstr), 3426 (N-H str) 2992 (C-Hstr).

**Compound TPI-10:**

Anal. Calcd. For C<sub>21</sub>H<sub>15</sub>N<sub>2</sub>Br: C,67.21; H, 4.03; N, 7.47; Br, 21.29 Found: C, 67.19; H, 4.09; N, 7.56; Br, 21.35 Yield (67%), ESI-MS 375.26(M+H); <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ 7.6 ppm (Ar-H, m), δ 11.9 ppm (Ar N-H, s), <sup>13</sup>C-NMR: δ 152 ppm (C=N), IR KBr (cm<sup>-1</sup>): 1630(C=Nstr), 1592 (C=Cstr), 3479 (N-H str) 3076 (C-Hstr).

From the observed spectroscopic data the proposed structure for the as-synthesized imidazole derivatives are shown below.

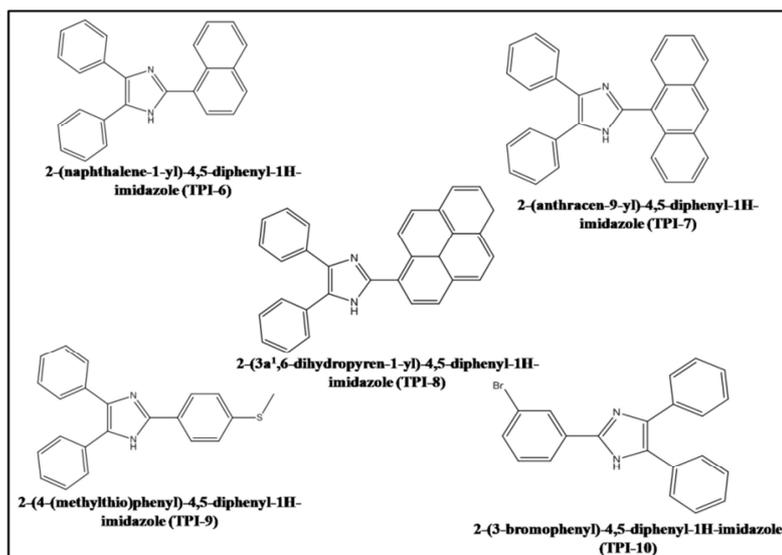


Fig 1. Proposed Structure of the synthesized imidazole derivatives

**Biological Evaluation****Antimicrobial activity**

The anti-microbial studies for the as synthesized given sample was carried out by disc diffusion technique. The synthesized compounds TPI-6, TPI-7, TPI-8, TPI-9 and TPI-10 with standard control were tested for its antimicrobial activity. The test is done to find out the effectiveness of the compound against pathogenic bacterial strains. Among the synthesized imidazole derivative TPI-7 shows maximum inhibition towards *Escherichia coli*, TPI-8 and TPI-10 shows comparatively equivalent inhibition towards *Pseudomonas aeruginosa*. TPI-9 shows less inhibition when compared to other synthesized compounds. TPI-6 shows maximum inhibition towards *Entobacter* sps.

**Antibacterial activity (Protocol)**

Antibacterial assay was done by disc diffusion method. The media Mueller Hinton agar was prepared for antibacterial study. The concentration of the given samples (5µg/disc) was applied on the sterile disc. 25µl of each sample was added to the sterile disc and placed on the agar plate. Ciprofloxacin was used as an antibacterial agent for the control. The incubation was carried out at 37 °C for 24 h. The diameters of the inhibition zones were measured in mm.

Table 2. Results of antimicrobial studies using the synthesized imidazoles

S.No.	Name of the Microorganisms	Mean zone of inhibition in Diameter (mm)					Standard Ciprofloxacin 5µg/disc (mm)
		TPI-6	TPI-7	TPI-8	TPI-9	TPI-10	
1	<i>Escherichia coli</i>	18	21	19	17	20	22
2	<i>Pseudomonas aeruginosa</i>	13	11	15	12	15	16
3	<i>staphylococcus aureus</i>	16	13	14	16	15	17
4	<i>Proteus vulgaris</i>	15	18	18	14	17	19
5	<i>Streptococcus pneumonia</i>	18	19	14	17	16	20
6	<i>Entobacter sps</i>	19	20	19	16	20	21

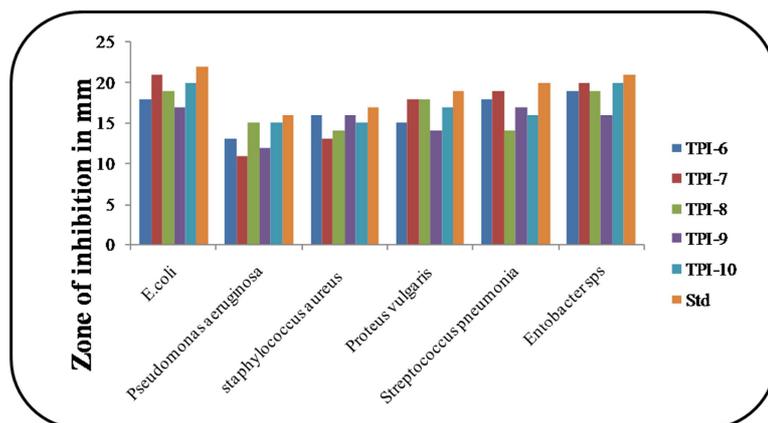


Fig 2. Zone of inhibition against the microorganisms by synthesized imidazoles

### CONCLUSION

In the present work, tri substituted imidazole derivatives were successfully prepared under catalyst free, environmentally benign route, the products obtained was purified by non – chromatographic techniques. The as-synthesized imidazole derivatives were characterized by FT-IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and Mass spectroscopy, The experimental results were found to be in good agreement with the reported literatures. From the experimental data the structure for the as-synthesized imidazole derivative was predicted. In addition, anti microbial activity of the as-synthesized imidazoles shows good inhibition against micro organisms.

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