



## An Efficient One-Pot Synthesis of Condensed Imidazoles Using Pentafluorophenylammonium Triflate as Novel, Metal-free and Reusable Catalyst

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A superior method of synthesis of condensed imidazoles by the catalytic action of pentafluorophenylammonium triflate on the reaction of 1,2-diaminoaromatics with orthoesters is described. The catalyst is reusable and can be applied several times without considerable decrease in the yields and rates of the reaction.

**Key Words:** Pentafluorophenylammonium triflate, Reusable, 1,2-Diaminoaromatic, Orthoester, Condensed imidazoles.

### INTRODUCTION

Benzimidazoles and imidazoles have received significant attention because of their biological activities such as antimicrobial<sup>1</sup>, antiparkinson<sup>2</sup>, anticancer<sup>3</sup>, antibiotic<sup>4</sup>, antifungal<sup>5</sup>, antihistaminic, antiparasitic, antiulcer, antihypertensive and antiviral<sup>6</sup> activities. They are used in diverse area of chemistry and are important intermediates in organic reactions. In addition, condensed imidazoles have been used as organic cations in ionic liquids<sup>7</sup>. The synthesis of fine chemicals following environmentally friendly strategies represents a challenging goal in the field of synthetic organic chemistry<sup>8</sup>. Because of the increasing importance of benzimidazoles<sup>9</sup> and imidazopyridines<sup>10</sup> in literature, a simpler approach to the synthesis of these heterocyclic systems other than those described before would be of great value. The extensions of heterogeneous catalysts for organic synthesis become a major area of research. The potential advantages of these materials over homogenous systems could lead to novel, environmentally benign chemical procedures for academia and industry<sup>11</sup>. Application of solid acids in organic transformations is important because they have many advantages including ease of products separation, recycling of the catalyst and environmental acceptability as compared to liquid acid catalysts<sup>12</sup>. Recently a variety of catalyst such as homogenous Lewis acid<sup>13</sup>, pyridinium-*p*-toluenesulfonate<sup>14</sup>, ionic liquid<sup>15</sup>, (bromodimethyl) sulfonium bromide<sup>16</sup>, poly-aniline sulfate<sup>17</sup> and tandem oxidation process<sup>18</sup> have been used for the synthesis of benzimidazoles. Saha and co-workers<sup>19</sup> have reported the synthesis of 2-substituted benzimidazoles in the presence of 1-methyl-3-pentylimidazolium tetrafluoroborate as solvent and catalyst. Funatomi *et al.*<sup>20</sup> reported the

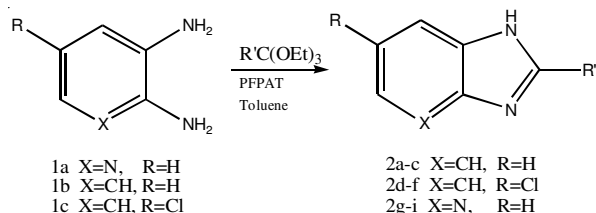
application of pentafluorophenylammonium triflate (C<sub>6</sub>F<sub>5</sub>NH<sub>3</sub> OTf; PFPAT) as a novel heterogeneous catalyst in organic transformation such as esterification of carboxylic acid with alcohols C-acylation of enol silyl ethers or ketone silyl(thio) acetals with acid chlorides<sup>21</sup> and Mukaiyama aldol and Mannich reaction using ketone silyl acetals with ketones and oxime ethers<sup>22</sup>. Very recently we reported our research findings on the application of pentafluorophenylammonium triflate (PFPAT) as a catalyst in the synthesis of coumarines *via* von pechman condensation<sup>23</sup>. However, there are no any reports about the application in catalyst is as a Brønsted acidic organocatalyst in the synthesis of condensed imidazoles.

### EXPERIMENTAL

**Synthesis of condensed imidazoles:** A mixture of 1,2-diaminoaromatic (1 mmol), orthoester (2 mmol) and pentafluorophenylammonium triflate (0.2 mmol) in toluene (3 mL) was refluxed with stirring for the indicated time (Table-2). The reaction mixture was monitored by TLC. After completion of the reaction, the reaction mixture, after being cooled to room temperature was poured onto crushed ice and stirred for 5-10 min. The solid product was collected by filtration under suction (water aspirator), washed with ice-cold water (25 mL) and then recrystallized from ethylacetate-hexane to afford pure material (Table-2). The filtrate was concentrated under reduced pressure and then recrystallized from hot hexane to recover the pentafluorophenylammonium triflate for subsequent use. All the compounds were identified by comparison of analytical data (IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR) and m.p. with the authentic samples.

## RESULTS AND DISCUSSION

Due to our interest in the synthesis of heterocyclic compounds<sup>24</sup> and in continuation of our previous work on the applications of reusable catalysts in organic reactions<sup>25</sup> herein we report a one-pot synthesis of benzimidazoles and imidazopyridines by the catalytic action of pentafluorophenylammonium triflate (PFPAT) on the reaction of 1,2-diamino-aromatics with orthoesters (**Scheme-I**).



**Scheme-I:** Synthetic route of condensed imidazoles

To initiation our study, the reaction of 1,2-diaminobenzene with triethylorthoformate were employed as a model reaction to examine the effect of various solvent, such as acetone, toluene, ethanol, methanol and chloroform and varying amount of pentafluorophenylammonium triflate (10, 15, 20 and 25 mol %). The use of acetone and chloroform gave the product (**2a**) in low yield (Table-1, Entries 2, 3). Ethanol and methanol gave moderate yields (Table-1, Entries 3, 4).

TABLE-1  
OPTIMIZATION OF VARIOUS SOLVENTS AND AMOUNT OF CATALYST FOR THE REACTION OF 1,2-DIAMINO-BENZENE WITH TRIETHYLORTHOFORMATE

Entry	Solvent	Catalyst (mol %)	Time (h: min) <sup>a</sup>	Yield (%) <sup>b</sup>
1	Toluene	-	5	-
2	Acetone	20	3	27
3	Chloroform	20	4	18
4	Ethanol	20	3	70
5	Methanol	20	4	64
6	Toluene	20	1:20	87
7	Toluene	25	1:30	86
8	Toluene	15	2	77
9	Toluene	10	2:30	72

<sup>a</sup>All reaction was carried out using PFPAT at reflux conditions;

<sup>b</sup>Isolated yields

Finally, the reaction in toluene with 20 mol % of catalyst afforded (**2a**) in 87 % yields (Table-1, Entry 6). Therefore, we selected toluene as solvent and 20 mol % of catalyst for this reaction. As shown in Table-1, no desirable products could be detected in the absence of catalyst for 5 h (Table-1, Entry 1); which indicated that the catalyst should be absolutely necessary for this reaction. To evaluate the generality of this model reaction we then prepared a range of condensed imidazoles under the optimized reaction conditions. In all cases the type of 1,2-diamino-aromatics and orthoesters had no significant effect on the reaction. The results are summarized in Table-2.

The reusability of the catalyst is one of the most important benefits and makes them useful for commercial applications, thus the recovery and reusability of pentafluorophenylammonium triflate was investigated. The pentafluorophenylammonium triflate catalyst was easily separated from the reaction mixture after work-up and recrystallized from hot hexane to give a pure pentafluorophenylammonium triflate for subsequent use. For example, the reaction of 1,2-diaminobenzene with triethylorthoformate, the corresponding benzimidazole in 87, 86 and 84 % isolated yield over three cycles.

## Conclusion

In conclusion, we have successfully demonstrated a novel and important catalytic activity of pentafluorophenylammonium triflate as an inexpensive, effective, reusable and non-corrosive catalyst for the synthesis of condensed imidazoles in high yields. In addition to its simplicity and mild reaction conditions, this method has the ability to tolerate a wide variety of substitutions in both components, which can afford different substituted benzimidazoles and imidazopyridines in high yield. The present practical method is a new candidate for synthetic chemists to apply for the synthesis of condensed imidazoles.

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TABLE-2  
SYNTHESIS OF IMIDAZOLE AND BENZIMIDAZOLE DERIVATIVES USING PENTAFLUOROPHENYLAMMONIUM TRIFLATE (PFPAT)<sup>a</sup>

Entry	R	R'	X	Product <sup>b</sup>	Times (h : min)	Yield (%) <sup>c</sup>	m.p. (°C)	
							Found	Reported
1	H	H	CH	2a	1:30	87	172-173	173-174[25e]
2	H	Me	CH	2b	1:45	88	175-176	175-176[25e]
3	H	Et	CH	2c	1:30	86	171-172	170-172[25e]
4	Cl	H	CH	2d	1:30	84	122-125	123-126[25e]
5	Cl	Me	CH	2e	2	86	198-200	199-200[25e]
6	Cl	Et	CH	2f	1:45	82	170-172	170-171[25e]
7	H	H	N	2g	2	89	149-151	150-152[9c]
8	H	Me	N	2h	2:30	83	189-190	189-190[25e]
9	H	Et	N	2i	2:30	87	139-140	138-139[25e]

<sup>a</sup>All reaction were carried out at reflux condition in toluene using 1,2-diamino-aromatics (1mmol), orthoester (2 mmol) and PFPAT (0.2 mmol).

<sup>b</sup>All the products were characterized by IR, <sup>1</sup>HNMR spectral data and comparison of their melting point with those of authentic samples. <sup>c</sup>Yields refer isolated pure product based on 1,2-diamino-aromatics

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