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# Studies of 2,4,5-trisubstituted imidazoles: Synthesis by using different catalysts and their biological activity

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## ABSTRACT

***The titled compound has been synthesized by using various catalysts such as $BiCl_3$, Glyoxylic acid, $InCl_3$, L-proline, $NaH_2PO_4$, $NH_4Cl$, Yb triflate and then the biological study of resulting substituted imidazole.***

**Keywords:** 2,4,5-trisubstituted imidazole, $BiCl_3$, Glyoxylic acid, $InCl_3$, L-proline, $NaH_2PO_4$, $NH_4Cl$, Yb triflate, biological study.

## 1. INTRODUCTION

The use of imidazoles and their derivatives in chemical processes, especially in pharmaceuticals, is becoming increasingly important, because of their possibility of hydrogen bond formation and not-shared electron pair of nitrogen atom of the imidazole cycle.

Among these imidazoles, 2,4,5-triphenylimidazoles can be used as light-sensitive materials in photography and known as inhibitors, fungicides and herbicides, plant growth regulators and therapeutic agents, and so on. They also show antinociceptive and anti-inflammatory activities.

$BiCl_3$ has found to be a mild and effective catalyst for the efficient, one-pot, three component synthesis of 2,4,5-triphenylimidazoles in RT. In recent years, bismuth compounds have been used as catalysts in organic synthesis because these compounds are relatively non-toxic, easy to handle, inexpensive, and possess good stability. Among these, $BiCl_3$ has gained special attention because not only is this compound commercially available and cheap, but also has high stability and is an environmentally friendly catalyst[1].

The use of microwave for the synthesis of organic compounds under solvent-free conditions proved to be efficient, safe and environmentally benign technique, with shorter reaction time, high yields, and easier manipulation. Additionally, it can also avoid the use of hazardous and expensive solvents and can be environmentally benign to make manipulations much easier[2].

Glyoxylic acid is a strong acid with extreme wide applications such as deportation of oximes, Diels-Alder reaction and very recently for the synthesis of 1,2-disubstituted bezimidazoles. So glyoxylic acid can be used for the synthesis of 2,4,4-triaryl imidazoles without any solvent under microwave irradiation[3].

In recent years, indium chloride has invoked enormous interest as a green and mild Lewis acid of high potential to construct carbon-carbon or carbon-heteroatom bonds in various organic transformations due to its low toxicity, cost effectiveness, air and water compatibility, ease of handling, good reactivity , experimental simplicity and excellent solubility in water and organic solvents. Moreover it has a remarkable ability to suppress side reactions in acid sensitive substrates[4].

L-proline(15 mol%) can be used as an organocatalyst for the efficient synthesis of 2,4,5-triphenylimidazoles in high yields[5].

The development of a new method for the synthesis of imidazole derivatives would be highly desirable. In recent years, $NaH_2PO_4$ has gained special attention as a catalyst in organic synthesis because many advantages such as excellent

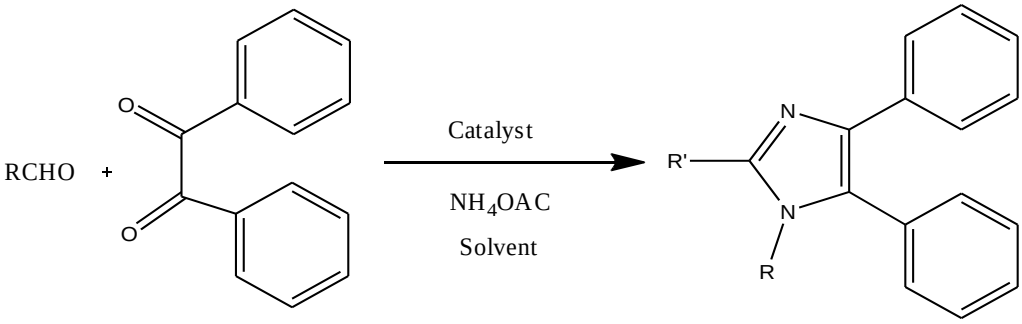
solubility in water, uncomplicated handling, inexpensiveness, eco-friendly nature, readily available and high reactivity[6].

$NH_4Cl$ was used as a catalyst for synthesis of organic compounds. For example ammonium chloride was applied in the synthesis of pyridines, the Claisen rearrangements of Ar-compounds, the reduction of azo compounds to corresponding hydrazines and the reduction of nitro-phenols. In 2009, Dr. Maleki's research group became successful to synthesize 2-aryl benzthiazoles by using $NH_4Cl$ as catalyst. Researchers reported solvent-free synthesis of 2,4,5-trisubstituted imidazoles using $NH_4Cl$ as a catalyst under classical heating[7].

Researchers examined a wide variety of Ar-aldehydes with various substituents to establish the catalytic importance of $NH_4Cl$ for this reaction. A wide variety of ortho-, meta- and para-substituted Ar-aldehydes undergo this one pot multi-component synthesis with Benzil or Benzoin and ammonium acetate to afford 2,4,5-trisubstituted imidazoles in good yields.

As a new type of Lewis acid, triflate been applied in a variety of organic reactions. The most characteristic feature of these rare earth metal triflates are that they act as water-compatible strong Lewis acids in aqueous solvents. Only catalytic amount of the catalysts is enough to complete reactions in most cases. Moreover, they can be easily recovered after reactions and reused without any loss of activity. Researchers have used lanthanide triflates for example $Yb(OTf)_3$ as catalyst in three component reaction for the synthesis of trisubstituted imidazoles.

## 2. EXPERIMENTAL




*ONE-POT MULTICOMPONENT SYNTHESIS OF IMIDAZOLE DERIVATIVES*

The use of different catalysts with their loading and solvent used and also the time required to obtain the substituted imidazole with their yield is mentioned in Table-I

1. **Table-I:** Effect of various catalysts

| Entry | Catalyst | Catalyst Loading (mol%) | Solvent | Time (hr) | Yield (%) |
|---|---|---|---|---|---|
| 1 | $BiCl_3$ | 0.4 mmol | Acetonitrile | 1 | 84-94 |
| 2 | Glyoxylic acid | 5 | Solvent-free (microwave) | 2 mins | 98 |
| 3 | $InCl_3$ | 10 | MeOH | 8.3 | 82 |
| 4 | L-proline | 15 | MeOH | 9 | 90 |
| 5 | $NaH_2PO_4$ | 10 mmol | Solvent-free | 7 mins | 93 |
| 6 | $NH_4Cl$ | 40 mmol | Solvent-free | 1 | 90 |

| | | | | | |
|---|---|---|---|---|---|
| 7 | Yb triflate | 5 | Acetic acid | 2 | 93 |

## 3. RESULTS AND CONCLUSION

These results indicate that The titled compound has been synthesized by using various catalysts such as $BiCl_3$, Glyoxylic acid, $InCl_3$, L-proline, $NaH_2PO_4$, $NH_4Cl$, Yb-triflate exhibit a high catalytic activity in the formation of substituted imidazoles in high yields in mild conditions, easy work-up, clean reactions profile, lower catalyst loading, cost efficiency and clean reaction profiles.Imidazole derivatives have a wide-ranging biological activity. The determination of antinociceptive activities of substituted imidazoles is based on hot plate and tail flick methods and anti-inflammatory studies are based on carageenaninduced paw oedema. Compounds with phenyl substitution with -F, -Cl, $-NH_2$, -OH and $-OCH_3$ at para position showed higher activity than all other substitutions. Electron donating and hydrophilicity play an important role in the biological activity. Lowering of activity was observed with hydrophobic groups. Quantitative-structure activity relationships are developed correlating the observed biological activity with structural descriptors[8].

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