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Title Key: Silver Iodide: An Efficient Heterogeneous Catalyst …

Silver Iodide: An Efficient Heterogeneous Catalyst for one Pot Synthesis of 2, 4, 5-Tri-substituted Imidazole

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Abstract

Silver iodide (AgI) is used as efficient, mild and water soluble catalyst for the synthesis of 2, 4, 5-tri-substituted imidazole by one pot three component condensation of benzil, an aldehyde and ammonium acetate in ethanol at reflux condition. The advantages of this method are mild reaction condition, simple procedure and solubility of catalyst in water for its removal from reaction mixture.

1. Introduction

Imidazole, a five member heterocyclic compound having nitrogen at 1 and 3rd position. Imidazole scaffold extensively represent variety of natural product such as histamine, histidine, biotin, alkaloids and nucleic acids. This imidazole scaffold is also found as constituents of various synthetic medicines. It shows various medicinal properties such as anticancer, anticoagulants, anti-inflammatory, antibacterial, antifungal, antiviral, antitubercular, antidiabetic and antimalarial. There are so many well prescribed drugs which contain imidazole moiety.

Imidazole was firstly synthesized by Radiszewski by condensation of dicarbonyl compound, benzaldehyde in the presence of ammonia to yield 2, 4, 5 tri-substituted imidazoles. Because of high medicinal values various synthetic methods are developed for synthesis of 2, 4, 5-tri-substituted imidazole via condensation of benzil, aromatic aldehydes and ammonium acetate in protonic acids, Lewis acids, silica supported acid and ionic liquids etc.

Most of these methods require prolong reaction time, harsh reaction condition affords low yield and shows difficulty in removal of catalyst from reaction Mass. AgI as catalyst found to be more efficient and water soluble in one pot synthesis of 2, 4, 5-tri-substituted imidazole.

Herein we report the one pot three component condensation of benzil, an aldehyde and ammonium acetate in ethanol using silver iodide as efficient and mild catalyst for the synthesis of 2, 4, 5-tri-substituted imidazole (Scheme-1).

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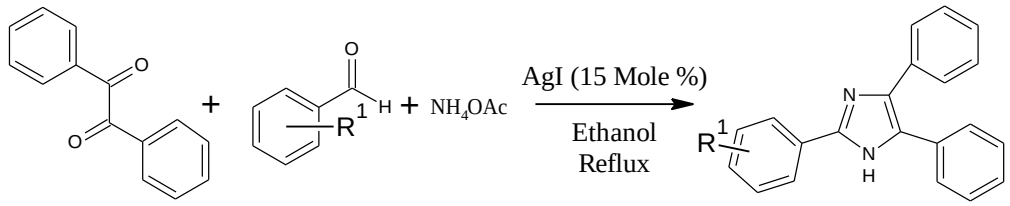

1 **2** **3(a-e)**

Scheme-1

2. General Procedure for synthesis of 2, 4, 5-Tri-substituted imidazole

A mixture of benzil (10 mmole), aldehyde (10 mmole) and ammonium acetate (30 mmole) was refluxed in ethanol using 15 mole % of AgI as catalyst to give 2, 4, 5 tri-substituted imidazoles. Reaction was monitored by using TLC on 10% ethyl acetate in n-hexane. On completion of reaction, the reaction mixture is cooled to room temperature and poured on crushed ice and stirred further for 30 minutes. The seperated crude product is purified by crystallization using ethanol as solvent. In case of anisaldehyde purification is carried out by using coloumn chromatography.

3. Result and Discussion

Optimization study is carried out by using model condensation reaction of benzil, an aldehyde and ammonium acetate in different conditions. Initially we have optimized the selection of solvent using catalyst AgI (20 mole %) by condensation of benzil, p-chloro benzaldehyde and ammonium acetate. Various solvent are used at reflux condition; but ethanol is found to be best solvent for such condition (Table-1).

Table-1: Optimization of solvent

Sr. No.	**Solvent**	**Time (hr)**	**Yield (%)**
1	Methanol	5	65
2	Ethanol	3.5	81
3	Acetonitrile	7	Impure sticky Reaction Mass
4	Water	12	Impure reaction mass

*A quantitative yield is obtained in ethanol as solvent and also less time required.

In optimization of mol % of catalyst required for reaction condensation of benzil, p-chloro benzaldehyde and ammonium acetate the reaction is carried out in ethanol solvent. A quantitative yield is obtained by using 15 mole % (Table-2).

Table-2: Optimization of catalyst concentration

Sr. No.	AgI %	Time (hr)	Yield (%)
1	10	5	70
2	15	3.5	81
3	20	3.5	77

In order to explore the application of this method several imidazole derivatives has been synthesized by using the same reaction protocol as listed in Table-3. The yield obtained is ranged between 69 to 81%. All the product are purified by using ethanol crystallization except for 3e purification. It was carried out by using column chromatography and mobile phase used is 5 % to 10 % ethyl acetate in n-hexane.

4. Conclusion

This method offer an alternative protocol for synthesis of 2, 4, 5-tri-substituted imidazole in mild reaction condition in one pot reaction, using water and ethanol as the green approach.

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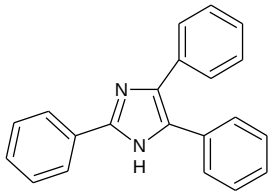
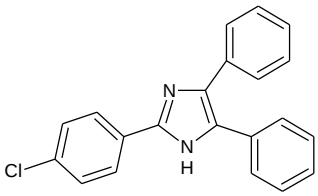
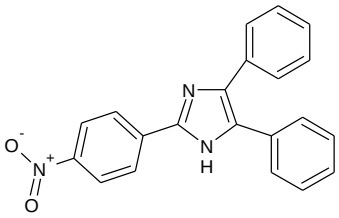
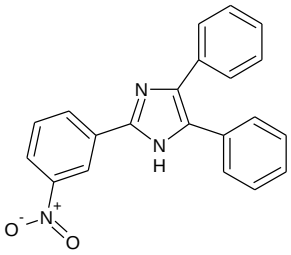
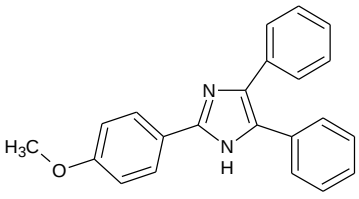
Table-3: Synthesis of various imidazole derivatives

Sr. No.	Compound	Yield	Time (hr)	M.P. (°C)
1	 3a	70 %	4.5	277
2	 3b	81%	3.5	261
3	 3c	79%	1.5	230
4	 3d	73%	2	<300
5	 3e	69%	6	230

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