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Research paper

## Ferric sulfate an Efficient Catalyst for the Synthesis of Imine under Solvent Free Condition

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**Abstract:** Anhydrous ferric sulfate has been found to be an efficient catalyst for the synthesis of imines. The reaction proceeds in high yields at ambient temperature and in short time. The reaction has been studied with a variety of carbonyl compounds and amines.

**Keywords:** Imine, Ferric sulfate, Amines, Carbonyl, Solvent free

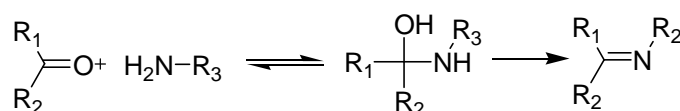
### INTRODUCTION

The nitrogen atom is present in many natural products, biologically important molecules, pharmaceuticals and dyes<sup>1</sup>. The condensation of amines with carbonyl compounds is a venerable and useful organic transformation<sup>2</sup> as the resultant imines are used as multifaceted components in nucleophilic addition with organometallic reagents<sup>3</sup>, in cycloaddition reactions<sup>4</sup> and have potential for therapeutic application such as lipooxygenase inhibitors, anti inflammatory agents<sup>5</sup> and anticancer agents<sup>6</sup>.

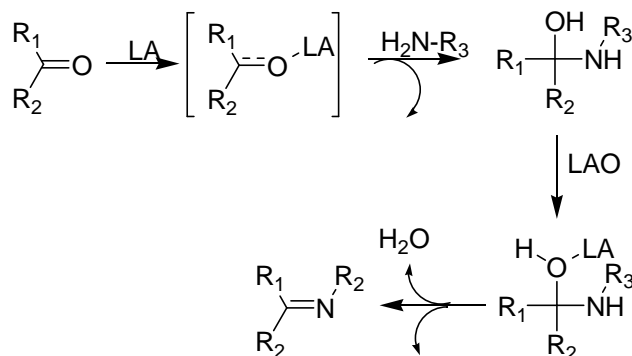
Several methods for the synthesis of imines are described in the literature; they can be obtained from aldehydes<sup>7</sup>, gem-dibromomethylaryl derivatives<sup>8</sup>, formamides<sup>9</sup> and by palladium catalyzed amination<sup>10</sup>. However, these methodologies often require complex procedures, long reaction times and large quantities of aromatic solvents. Various synthetic routes for the synthesis of imines are depicted in **scheme-1**<sup>22</sup> As nucleophilic attack by the amine at the carbonyl carbon in the first step is reversible, the feasibility of imine formation largely depends on the rate of removal of water in the final step (route A). The classical synthesis of imines, originally reported by Schiff<sup>11</sup> involves condensation of a carbonyl compound with an

amine under azeotropic distillation to separate the liberated water<sup>12</sup>; its subsequent removal was facilitated by the use of molecular sieves<sup>13</sup>. Recently an in situ dehydration strategy has been adopted by the use of dehydration solvents such as tetramethyl orthosilicate<sup>14</sup> and trimethyl orthofomate<sup>15</sup>. In an alternative approach (route B), the condensation reaction has been carried out in the presence of ZnCl<sub>2</sub><sup>16</sup>, TiCl<sub>4</sub><sup>17</sup>, MgSO<sub>4</sub>-PPTS<sup>18</sup>, alumina<sup>19</sup>, K-10 under microwave irradiation<sup>18,21</sup>, Ti (OR)<sub>4</sub><sup>19</sup> which act as Lewis acids to catalyze nucleophilic attack on the carbonyl group by the amine as well as serve as dehydrating agents to facilitate the removal of water in the final step. *Chakraborti et.al.* reported the synthesis of imines using magnesium perchlorate as the catalyst with reaction times ranging from 15 to 480 min.<sup>22</sup>

Route A:



Route B:



**Scheme 1: Routes for synthesis of imines**

The methodologies reported to have disadvantages in terms of high reaction temperatures, prolonged reaction periods, and excess of expensive dehydrating reagents/catalysts, moisture sensitive catalysts, and special apparatus. Moreover, the efficiency of the procedures reported is limited to the reaction of highly electrophilic carbonyl compounds and strongly nucleophilic amines.

Ferric sulfate is inexpensive, non-toxic to the environment and easily available. Ferric sulfate is used as efficiently Lewis acid in Knoevenagel condensation<sup>23</sup>, the Ferrier reaction of per-O-acetylated/benzylated glucoses with alcohols to give 2,3-unsaturated α-glycosides in a few minutes under microwave irradiation<sup>24</sup> an efficient heterogeneous catalyst for the tetrahydropyranlation of alcohols and phenols at ambient or near ambient temperature<sup>25</sup>. Here we report an efficient, practical environmentally benign and high yielding method for the synthesis of imines using Ferric sulfate as catalyst.

## EXPERIMENTAL

All purchased chemicals were of analytical grade and used without further purification. The <sup>1</sup>H NMR spectra were obtained on a Bruker DRX-300 Avance instrument using CDCl<sub>3</sub> as solvent and TMS as internal standard at 300MHz. All products are known compounds; their physical and spectroscopic data were compared with those reported in the literature and found to be identical.

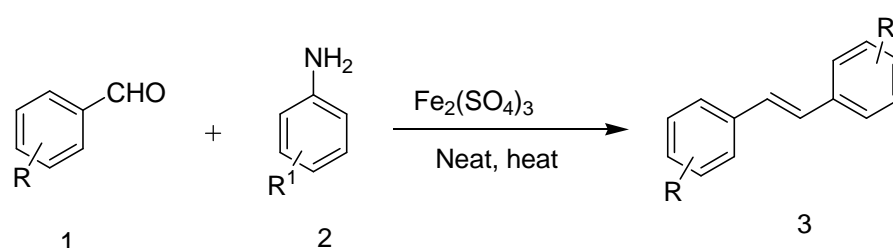
**Typical Procedure for imine formation:** A mixture of Substituted benzaldehyde (1mmole) Or Indole 3-Formaldehyde (1mmole), Substituted aniline (1 mmole) and ferric sulfate (0.5mmol) was heated in neat

condition at 50°C for 2-3 hrs. Progress of the reaction was monitored by TLC. After completion of the reaction, ice cold water was added into the reaction mixture, solid is precipitated out, filtered on Buckner funnel washed with water and ice cold ethanol.

## RESULTS AND DISCUSSION

We thought that the condensation between a carbonyl compound and an amine leading to the formation of an imine should be a facile reaction due to the good electrophilic and nucleophilic properties of the carbonyl and amine groups, respectively, and may not require any catalytic assistance in the absence of electronic factors. But when the electrophilicity of the carbonyl and nucleophilicity amino groups might be decreases require catalyst for the condensation of carbonyl and an amino group. Ferric sulfate is used as efficiently Lewis acid in many organic transformations. Ferric sulfate co-ordinate with carbonyl oxygen and increase the electrophilicity of the carbonyl group and facilitate the nucleophilic attack of amine on carbonyl and serve as dehydrating agents to facilitate the removal of water in the final step.

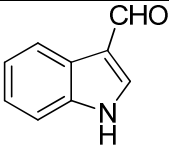
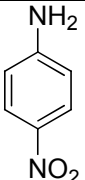
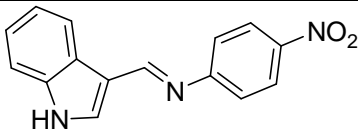
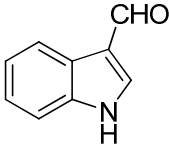
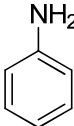
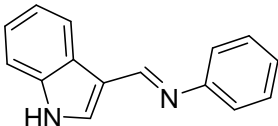
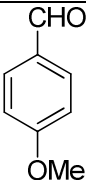
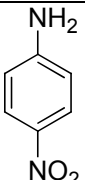
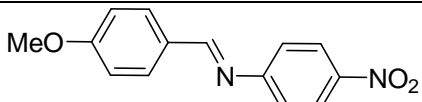
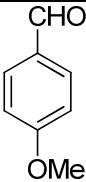
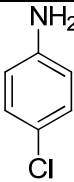
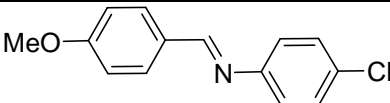
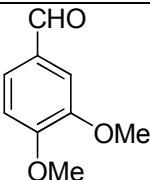
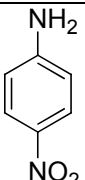
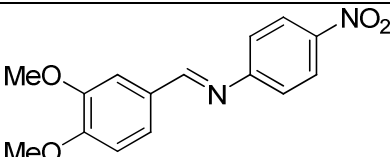
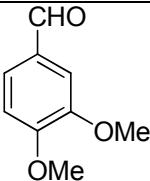
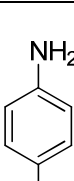
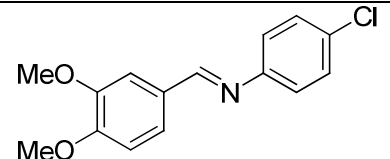
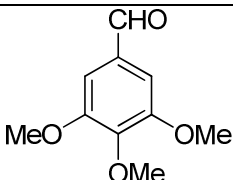
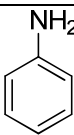
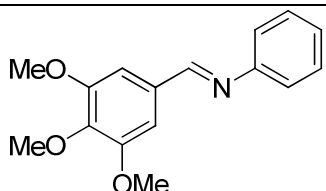
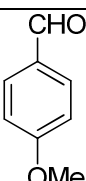
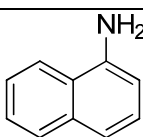
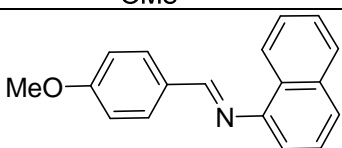
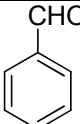
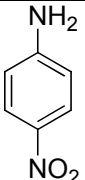
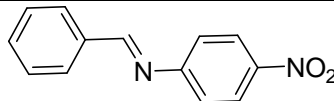
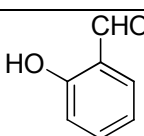
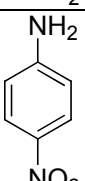
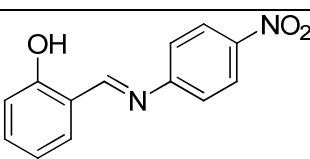
To establish the scope and limitations of Ferric sulfate as a catalyst for imine formation, structurally diverse carbonyl compounds were treated with different amines such as aniline, 4-chloroaniline, 4-nitroaniline under the catalytic influence of Ferric Sulphate and the results are summarized in table1. Excellent results are obtained in most cases.

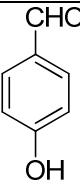
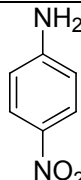
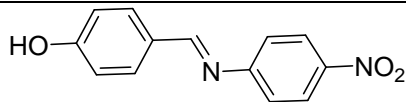
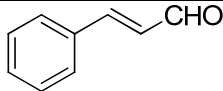
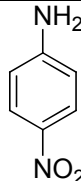
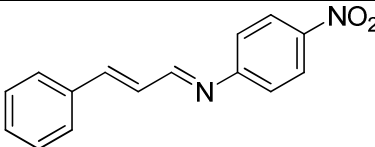
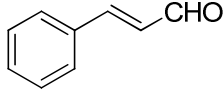
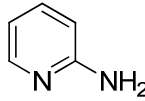
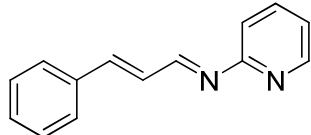


**Scheme 2: Synthesis of imines catalyzed by Ferric sulfate under solvent free condition**

**Table-1: Ferric sulfate catalyzed synthesis of imines**

Sr. No.	Aldehyde R	Amine R <sup>1</sup>	Product	Yield <sup>b</sup> (%)
1.				90
2.				96
3.				98

4.				96
5.				92
6.				82
7.				92
8.				92
9.				90
10.				91
11.				88
12.				85
13.				83

14				82
15				89
16				87

**b: isolated yield**

## CONCLUSION

In summary, the present procedure for use of ferric sulfate as an efficient catalyst for synthesis of imines offers advantage in terms of inexpensive and easily available catalyst, condensation of deactivated amines and carbonyl compounds to afford imines in high yields compared to reported methods, reaction conditions and work up procedure are mild and easy to handle and avoid the use of organic solvent. The present eco-friendly procedure represents an alternative to the existing methods for synthesis of imines.

## ACKNOWLEDGEMENTS

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