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Hemoglobin/ Ferrous ammonium sulphate catalyzed green synthesis of Triarylimidazoles

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ABSTRACT

A green and efficient method, using Hemoglobin and Ferrous ammonium sulphate was developed for the synthesis of 2,4,5-triaryl-1*H*-imidazoles devoid of solvent. The synthesized compounds were characterized by spectral analyses.

KEY WORDS: Multicomponent Reactions, Imidazoles, Ferrous Ammonium Sulphate and Hemoglobin.

1. INTRODUCTION

Multicomponent reactions (MCRs) have much importance as they are prevailing tool for synthesis of many multifaceted organic compounds (Weber, 2002; Hulme and Gore, 2003; Tempest, 2005; Domling, 2006; D'Souza and Müller, 2007; Duque, 2010). They are also one-pot processes bringing together three or more components in a particular series of reactions and demonstrate elevated atom financial system and significant selectivity. Since, their preparation is trouble-free; MCRs have engaged a very important position in multiplicity oriented synthesis which is an essential prerequisite for drug innovation. Imidazole is a significant class of organic compound being the most important components of many naturally occurring products, as well as synthetic derivatives. These molecules have great importance due to their useful biological and pharmacological aspects. They act as inhibitors of p38 MAP kinase (Vatter, 1994), B-Raf kinase (Takle, 2006), transforming growth factor b1 (TGF-b1) type 1 actin receptor-like kinase (ALK5) (Khanna, 1997), cyclooxygenase-2 (COX-2) (Lange, 2005) and biosynthesis of interleukin-1 (IL-1) (Gallagher, 1995). Suitably substituted imidazoles are expansively used as glucagon receptors (De Laszlo, 1999) and CB1 cannabinoid receptor antagonists (Eyers, 1998), modulators of P-glycoprotein (P-gp)-mediated multidrug resistance (MDR) (Newman, 2000), antitumor (Wang, 2002) and Antibacterial agents (Antolini, 1999). Many reports on synthesis of triaryl-1*H*-imidazoles reveal less yield, more reaction time ant product needs further purification, where as in this report we achieved good results in terms of yield, simple method for synthesis. The product obtained needs no further purification.

2. EXPERIMENTAL

The chemicals used were commercially available from Merck or Fluka and were used as such. However when needed were purified using normal techniques. Melting points were taken on a melting point apparatus and are uncorrected. FTIR spectra, ^{1}H NMR spectra and Mass spectra were obtained from the Indian Institute of Chemical Technology, Hyderabad, India.

Synthesis of triarylimidazoles:

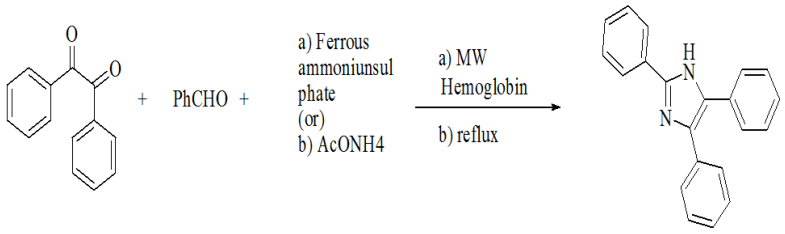
Method a: A mixture of benzil (0.525 g; 2.5 mmol), benzaldehyde (0.5 mL; 2.5 mmol), ammonium acetate (0.5 g; 6 mmol) and Hemoglobin powder (0.05 g) was irradiated under microwave for 5 min. After completion of the reaction, the reaction mixture was filtered to get 2,4,5-triphenyl-1*H*-imidazole.

Method b: A mixture of benzil (0.525 g; 2.5 mmol), benzaldehyde (0.5 mL; 2.5 mmol), Ferrous ammonium sulphate (0.5 g; 6 mmol) was irradiated under microwave for 5 min. After completion of the reaction, the reaction mixture was filtered to get 2,4,5-triphenyl-1*H*-imidazole.

Method c: A mixture of benzil (0.2625 g; 1.25 mmol), benzaldehyde (0.25 mL; 1.25 mmol), ammonium acetate (0.231 g; 3 mmol) and Hemoglobin powder (0.05 g) was irradiated under microwave for 5 min. The reaction mixture was then poured into water; precipitates of 2,4,5-triaryl-1*H*-imidazole formed were filtered, washed with cold ethanol-water mixture and dried.

Method d: A mixture of benzil (0.525 g; 2.5 mmol), benzaldehyde (0.5 mL; 2.5 mmol), Ferrous ammonium sulphate (0.5 g; 6 mmol) was heated on a boiling water-bath for 2 hrs. The reaction mixture was then poured into water; precipitates of 2,4,5-triaryl-1*H*-imidazole formed were filtered, washed with cold ethanol-water mixture and dried well.

2,4,5-Triphenyl-1*H*-imidazole (1a): m.p.172 ºC. FTIR (cm^{-1}): 3427, 3062, 1668, 1589, 1492, 1450, 1418; ESI MS (m/z): 296 (M^+); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07-8.16 (m, 2H), 7.95-8.0 (m, 3H), 7.63-7.70 (m, 2H), 7.43-7.57 (m, 7H), 7.30-7.36 (m,2H)



Scheme 1: Synthesis of Triaryl imidazoles

3. RESULTS AND DISCUSSION

The compound formed was characterized by spectral analysis. IR spectra of the compound showed the N-H stretching frequency in the region 3400-3500 cm-1 which confirmed the presences of (N-H) amine group. The condensation of mixture of benzil and substituted benzaldehyde along with ammonium acetate were carried out at 80 ^{0}C under reflux. Based on careful analysis of the literature and comparison of the results for the synthesis of triphenyl imidazole(s) as a model reaction, we have tried synthesis with other catalyst. One of the major advantage of using Hemoglobin as catalyst is the ease of purification of the desired product. Hemoglobin can be easily eliminated during work-up and purification. The reactions were also carried out under reflux for 2 hours, which lead to very poor yield (40 %) of the product. The reactions were also carried out under MW in the absence of catalyst to enhance yield of the product with no appreciable increments in the yield. The present investigation is demonstrated that presence of the catalytic amount of Hemoglobin resulted excellent yields (90%). In the subsequent method, ferrous ammonium sulphate was used as one of the reactants in the place of ammonium acetate to give the desired product. Here too the product was obtained in good yields (80%). Both the methodologies employed were green synthetic procedures and were environmental friendly.

4. CONCLUSION

In conclusion, we have shown that, Hemoglobin is an excellent catalyst for the multi-component one pot synthesis of 2, 4, 5,-triaryl-1H-imidazoles. The advantage of the reported method are the use of cheap, mild and easily available catalyst, easy work up and better yields.

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