



**TRIFLUOROACETIC ACID: AN EFFECTIVE CATALYST FOR THE GREEN ONE-POT  
SYNTHESIS OF TETRASUBSTITUTED IMIDAZOLES UNDER MICROWAVE  
ASSISTED SOLVENT FREE CONDITIONS**

**M.R. Mohammadizadeh, A. Hasaninejad, M. Bahramzadeh**

*Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169, Iran*

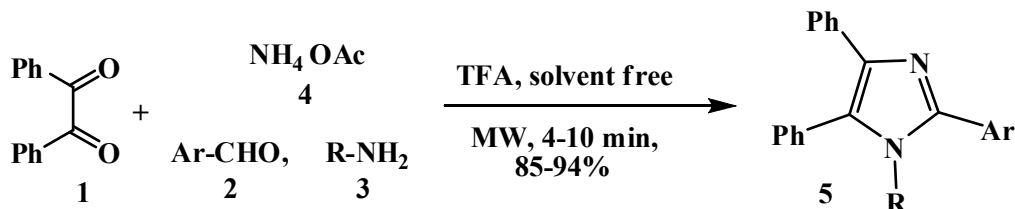
*mrmohamadizadeh@pgu.ac.ir*

The multi-component coupling reactions are emerging as a useful source for accessing small drug-like molecules with several levels of structural diversity. They are welcome too in terms of economic and practical considerations.<sup>1</sup>

The imidazole moiety, as part of the side chain in histidine, plays a major role in the biological functions of many peptides and proteins. Functionalized imidazoles also comprise an important class of pharmacologically active compounds with a wide range of interesting properties. Members of this class of compounds are known to possess NO synthase inhibition and antifungal, antimycotic, antibiotic, antiulcerative, and CB1 receptor antagonistic activities. Consequently, methodologies for the preparation of imidazoles have attracted much attention from both industry and academia, and numerous solution-phase syntheses of these compounds have been reported.<sup>2</sup>

On the other hand, there is an increasing interest in the use of environmentally feasible reagents particularly in solvent-free conditions. Prevention of organic solvents during reactions in organic synthesis leads to a clean, efficient, and economical technology; not only with the increment of safety, the simpleness of work up, and the reduction of cost, but also increased amounts of reactants can be achieved in the same equipment without huge modifications. Reactivity and sometimes selectivity may be enhanced without dilution.<sup>3</sup>

Following our previous works on the using of acidic catalysts for synthesis of organic compounds,<sup>4</sup> here we report the one-pot four-component condensation of benzil, benzaldehyde derivatives, primary amines and ammonium acetate for synthesis of tetrasubstituted imidazoles using trifluoroacetic acid (TFA) under solvent free conditions (Scheme 1).



Scheme 1

### References:

1. (A) Ramon, D. J.; Miguel, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602; (B) Orru, R. V. A.; de Greef, M. *Synthesis* **2003**, 1471; (C) Ugi, I.; Heck, S. *Comb. Chem. High Throughput Screening* **2001**, *4*, 1.
2. Balalaie, S.; Arabanian, A. *Green Chem.* **2000**, *2*, 274 and references cited there in.
3. (a) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025; (b) Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225.
4. Azizian, J.; Mohammadi, A. A.; Karimi, A. R.; Mohammadizadeh, M. R. *J. Org. Chem.* **2005**, *70*, 350.