



# Three-Component Coupling of Amines, Aldehydes and Aliphatic Halides Under Barbier-like Conditions in Water

Idália Helena Estevam<sup>a</sup>, Suelen Lins<sup>a</sup>, Veronica Conceição<sup>a</sup>

<sup>a</sup>Departamento de Ciências Exatas e da Terra, Universidade do Estado da Bahia, Salvador-BA

\*iestevam@uneb.br

**Keywords:** Iminium, aromatic amine, zinc

## INTRODUCTION

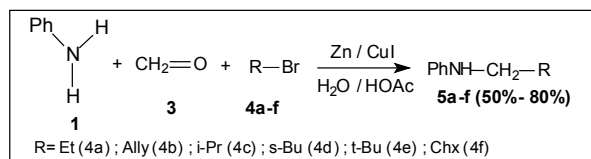
Multicomponent reactions in water are an important method in organic synthesis. One of the benefits of Green Chemistry is atom economy and safe solvent. Based on this some secondary and tertiary amine have been prepared in an aqueous medium in good yields.<sup>1</sup> Wei and co-workers<sup>2</sup> have obtained some propargylamines by coupling aldehydes, alkynes and amines in water in good yields.

Aromatic amines are important building blocks for a broad range of biologically active compounds, and intermediate to dyes and pigments.<sup>3</sup>

In previous work,<sup>4</sup> our group synthesized homoallylic amines from coupling reaction between secondary amines, methanal and halides in high yields. Herein we report the synthesis of aromatic amines in water with iminium from aniline and methanal.

## RESULTS AND DISCUSSION

Our study is mainly based upon the use of water as solvent in organic synthesis. The method consists of a one-pot reaction in microscale by mixing aniline, methanal, acetic acid, halide, zinc and CuI at room temperature by 60min. (Figure 1)



**Figure 1.** Three-Component Coupling of Amines, Aldehydes and Aliphatic Halides

The studies for the synthesis of amines were performed in two steps. Initially, to optimize the experimental conditions for the reaction, was made a series of experiments, varying quantities of acid (1 and 2mmol), catalyst (10% and 30% mol), metal (1,5 and 2,5 mmol) and halide (2 and 3mmol). The best conditions were selected by the TLC observation results.

To verify the generality of the reaction, different halides **2a-f** were tested under the optimized reaction conditions and successfully transformed on anilines derivatives. The products were confirmed

by GC-MS and NMR. No tertiary amine was observed in the chromatograms.

**Table 1.** Coupling of iminium from aniline and methanal to different halides<sup>a</sup>

Entry	Amine	Halide	Product	Yields <sup>b</sup>
1				70
2				80
3				73
4				75
5				50
6				50

<sup>a</sup> Condition: 1mmol of aniline, 1 mmol of acetic acid, 1,5 mmol of methanal, 2mmol of alkyl halide, 1,5 mmol of granulated zinc, 30% mol of CuI, 60min.

<sup>b</sup> isolated yields

## CONCLUSION

Aromatic amines were obtained under mild conditions and good yields. The method presents the substitution of organic solvents by water for synthesis of aromatic amines. The reaction time is shorter than the usual methods for obtaining aromatic amines.

## ACKNOWLEDGEMENTS

PGQA-UNEB ; PPG-UNEB; FAPESB; AGILENT

## REFERENCES

- Kumaravel, K., Vasuki, G. *Curr. Org. Chem.* **2009**, *13*, 1820.
- a) Wei, C., Li, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9584. b) Shen, Z. L., Loh, T. P. *Org. Lett.* **2007**, *9*, 5413.
- Jia, J. H., Sheng, W. J., Han, L., Tu, J. F. *Sci China Ser B* **2009**, *52*, 2171.
- Estevam, I. H. S., Bieber, L. W. *Tetrahedron Lett.* **2003**, *44*, 667.