Mild Transition Metal-Free Ipso Substitution using Amines and Thiols on Electron-Deficient Aryl Benzotriazolyl Derivatives

Asmita Sikdar, Sandip Mondal and Bhubaneswar Mandal\*

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati-781039, India.

E-mail: [bmandal@iitg.ac.in](mailto:bmandal@iitg.ac.in)

**Abstract**

The aryl amine and aryl thioether moiety are very often present in natural products and medicinal chemistry. Moreover, these aryl amines play an essential role in many commercial fine chemicals industries, polymer, and dye sectors. Many known drugs contain these arylamines and thioether functionality. For example, Norfloxacin is an antibacterial used to treat inflammation of the prostate gland and urinary tract infection, Tolfenamic acid is used as an anti-inflammatory agent, Linezolid is a vital antibiotic, and Vortioxetine is an antidepressant. There are numerous procedures established for both the arylation of amine and thiol by classical SNAr reaction or coupling reaction with the help of transition metal catalyst.1 Here, we have developed a simple, convenient strategy for the arylation of amine and thiol on aryl benzotriazolyl derivatives without using toxic transition metal catalysts. Aryl benzotriazolyl derivative is formed from corresponding benzene sulfonyl chloride and 1-hydroxybenzotriazole (HOBt), which shows desmotropic nature and may exist in three different forms.2 These aryl benzotriazolyl derivatives react with amine and thiol to produce arylated products with excellent yield (upto 99%). This method neither requires an expensive, toxic transition metal catalyst nor harsh reaction conditions.



**Scheme 1**: Schematic diagram of arylation of amine and thiol

**Key words:** Ipso-substitution, green method, transition-metal free, N and S arylation

**References:**

1. Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.,* **2004**, *248*, 2337-2364.

2. Barlos, K.; Papaioannou, D.; Theodoropoulos, D. *Int. J. Pept. Protein Res*., **1984**, *23*, 300–305.