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A Simple and Efficient Approach for the Synthesis of 2-Aminated Quinazoline Derivatives via Metal Free Oxidative Annulation

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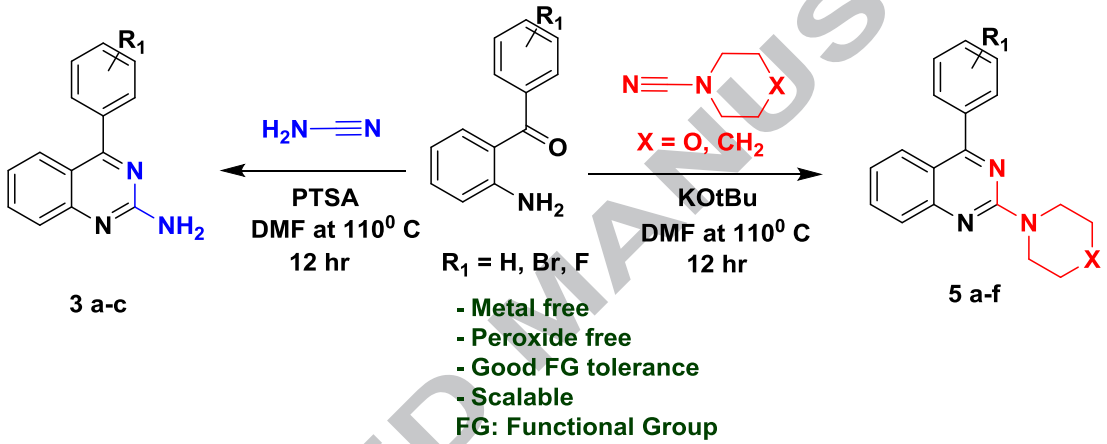
Abstract



A simple and efficient approach for the synthesis of 2-aminoquinazoline derivatives in moderate to good yields. This reaction employs mild reaction conditions, is metal-free and utilizes readily available starting materials making it a more viable reaction for the scale up synthesis and ligand diversity. Notably, this methodology allows the synthesis of 2-aminoquinazolines using a free amine or cyclic amine enabling structural diversity and good atom economy.

Keywords: Quinazolines / Oxidative Annulation / Metal Free / Heteroaromatic

Designing a simple and efficient chemical reaction sequence that provides maximum structural diversity with few synthetic steps to yield small heterocyclic molecules with interesting biological function is a challenge to both medicinal and synthetic chemists.[1] As a representative of heterocyclic molecules, 2-aminoquinazolines are drug-like scaffolds and exhibit wide range of biological activities such as potent, selective, and orally efficacious inhibitors of receptor tyrosine kinase c-Kit, represented by the 5,6-dihydro-pyridinone **1**[2] along with a 2¢-deoxynucleotide analogue **2**[3] (figure 1). The 2-aminoquinazoline and quinazoline scaffold is also represented in FDA-approved pharmaceuticals including the antihypertensive agent Prazosin **(3)** and the anti-cancer agent Gefitinib **(4)** (figure 1).