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Microwave-assisted Groebke-Blackburn-Bienaymé multicomponent reaction to synthesize imidazo fused heterocycles via in-situ generated isocyanides from *N*-formylamines: An undergraduate organic laboratory experiment

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Abstract

A one-pot methodology is developed for the direct conversion of *N*-formylamine, 2-amino pyridine, and aldehyde into 2,3-substituted imidazo [1,2-*a*]pyridine heterocycles using I_2-PPh_3-Et_3N reagent system under microwave irradiation. During the reaction, I_2-PPh_3-Et_3N converts *N*-formylamine into isocyanide, which in the presence of in-situ generated hydrogen iodide (HI) undergoes Groebke-Balckburn-Bienaymé (GBB) multicomponent reaction with aldehyde and 2-aminopyridine. The in-situ generated HI eliminates the need for an external catalyst for the GBB reaction. The developed process incorporates the use of readily accessible and cheap reagents and also avoid a separate step for the synthesis of isocyanides having disagreeable odor. Fourteen different GBB based heterocycles have been synthesized to demonstrate the feasibility of the optimized protocol. The preparation of *N*-formylamines utilized in the synthesis is also elaborated and the overall process was optimized to be suitable for a typical undergraduate organic laboratory experiment. One of the final products was characterized using FT-IR, ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HSQC, HRMS, and single-crystal X-ray diffraction. Overall, the experiment will be useful in the organic chemistry curriculum to teach about multicomponent reactions, the importance of isocyanides in organic synthesis, formylation of amines, application of microwave irradiation in organic synthesis, and structural elucidation of small organic molecules.

1 | INTRODUCTION

Multi-component reaction (MCR) is an organic transformation in which more than two substrates react together in one step to generate a final product, which carries almost the whole structural unit of the reactants with minimum side products (such as water). The formed products exhibit a wide range of structural diversity, which can be either used as a precursor for a particular synthetic transformation or as a final product for various

