ChemPubSoc Europe

DOI: 10.1002/slct.201702677

Chemistry SELECT Full Papers

Organic & Supramolecular Chemistry

A Facile, Convenient and Catalyst-Free One-Pot Route to Fluorescent Pyrrolo[3,4-*c*]pyridines via Multicomponent Strategy in Aqueous Medium

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A unique, convenient and efficient multicomponent one-pot synthetic approach to access a wide variety of pyrrolo[3,4-*c*] pyridines has been developed. This is the first report of the direct synthesis of pyrrolo[3,4-*c*]pyridine amido-triones from primary amines, malononitrile and dialkylacetylenedicarboxylate in an aqueous medium without using any catalyst. The newly synthesized compounds are fluorescent in nature and photophysical properties of some selective compounds have been carried out. In addition, a comparative photophysical study of some selective fluorophores was also performed in a wide variety of solvents.

Introduction

Multicomponent reaction[1] is an elegant synthetic route to mimic diverse molecular skeleton of fused heterocycles of interest.[2] Fused heterocyclic rings[3] are pharmaceutically important scaffolds because of their ease of availability in natural products e.g. alkaloids,[4] along with their wide array of biological activities including HIV-1 integrase inhibition,[5] multidrug resistance (MDR) reversal in cancer cell lines,[6] cytotoxicity,[7] or immunomodulation[8] etc. In this regard, pyrrole fused heterocyclic rings[9] being an important intermediate for many syntheses, are of immense importance in the convenient synthesis of different biologically active compounds.[10] In particular, the introduction of heterocycles in pyrrolo[3,4-*c*] pyridine could enhance its analgesic, hypotensive, psychotropic and other biological effects.[11] It is worth mentioning that, pyrrolo[3,4-*c*]pyridine core also acts as antimycobacterial,HIV-1integrase inhibitor and GPR119 agonist (Figure 1).[12] However, till date, there are only few reports of such core unless they are synthesized *via* multi-step reactions. The synthesis of such cores has been carried out either in acid, base or in presence of other catalysts.[13] Thus, an efficient straightforward synthetic strategy that transforms the commercially available substrates directly to the desired substituted pyrrolo[3,4-*c*]pyridine is still very much in need. Hence, we took an interest to synthesize the pyrrolo fused pyridine with 1, 3, 6-tricarbonyl system from easily available starting materials in a single step through multicomponent reaction. After a long journey, we have disclosed an efficient, one-pot, three-component synthesis of the desired core using malononitrile, dialkyl acetylenedicarboxylate and primary amine as the starting materials in aqueous medium. Water is undoubtedly the most obvious material of choice for any 'clean' reaction. The synthesis of this fused heterocyclic core in water would thus be an interesting addition to the multicomponent reaction toolbox. This multicomponent reaction is of high efficiency as it affords a broad substrate scope even in absence of catalyst. Thus, in this paper, it is the first report where the pyrroledione is fused with N-substituted 6-pyridone resulting in a series of new compounds. The substituted pyridines show fluorescence activity that leads us further to explore their photophysical properties considering the growing interest in small molecule organic fluorophores.[14]

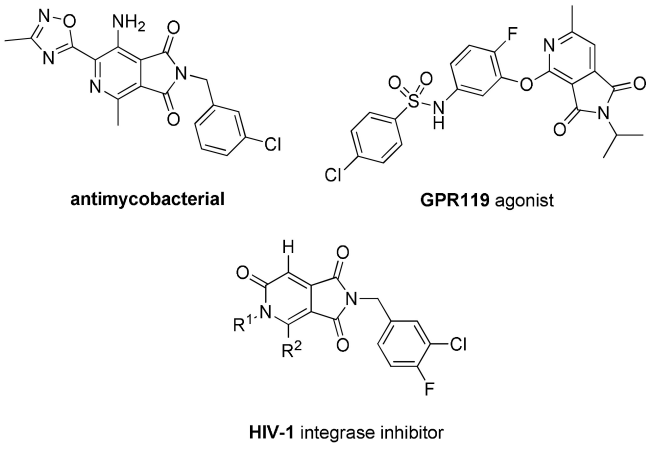

Figure 1. Biological activity of pyrrolo[3,4-*c*]pyridines.

Results and Discussion

We have evaluated the three component reaction of 1:1:1 mixture of aniline (**1a**), malononitrile (**2**), and dimethyl acetylenedicarboxylate (**3**) under various conditions. Initially, we

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Supporting information for this article is available on the WWW under https://doi.org/10.1002/slct.201702677