Tetrahedron 69 (2013) 1074–1085

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Potassium phthalimide-*N*-oxyl: a novel, efficient, and simple organocatalyst for the one-pot three-component synthesis of various 2-amino-4*H*-chromene derivatives in water

Mohammad G. Dekamin *, Mohammad Eslami, Ali Maleki

Pharmaceutical and Biologically-Active Compounds Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran 16846-13114, Iran

ARTICLE INFO

Article history:
Received 29 August 2012
Received in revised form 2 November 2012
Accepted 20 November 2012
Available online 28 November 2012

Keywords:
Potassium phthalimide-*N*-oxyl (POPINO)
Transition metal-free catalysis
Multi-component reactions (MCRs)
2-Amino-4*H*-chromene
Green chemistry

ABSTRACT

A wide variety of 2-amino-4*H*-chromene derivatives with diverse substituents on the 4*H*-chromene ring were efficiently prepared via one-pot, three-component reaction of an aromatic aldehyde, malononitrile (or ethyl cyanoacetate), and diverse enolizable C–H activated acidic compounds in the presence of low loading of potassium phthalimide-*N*-oxyl (POPINO), as a new organocatalyst, in aqueous media. This procedure is a clean, transition metal-free, and environmentally friendly approach to prepare different 2-amino-4*H*-chromen derivatives that offers many advantages including short reaction time, high to quantitative yields, low cost, and straightforward work-up.

1. Introduction

Multi-component reactions (MCRs) have emerged as an attractive and powerful strategy for organic synthesis compared to multi-step reactions due to the creation of several new bonds in a one-pot reaction, low number of reaction and purification steps, selectivity, synthetic convergence, high atom economy, simplicity, and synthetic efficiency.[1] Therefore, academic and industrial research groups have increasingly focused on the use of MCRs to synthesize a broad range of products.[2] In fact, development of MCRs can lead to new efficient synthetic methodologies to afford many small organic compounds in the field of modern organic, bioorganic, and medicinal chemistry.[1–3] Hence, MCRs are considered as a pivotal theme in the synthesis of many important heterocyclic compounds such as chromene derivatives nowadays. The chromene moiety, including that of 2*H*-chromene and 4*H*-chromene, belongs to a major class of natural oxygen-containing heterocyclic compounds, which are widely found in edible fruits and vegetables.[4] These compounds have occupied an important place in drug research because of their various biological and pharmacological activities such as antioxidant, antileishmanial, antibacterial, antifungal, hypotensive, anticoagulant, antiviral, diuretic, antiallergenic, and antitumor activities.[5] Generally, the biological and pharmacological activities of chromenes depend on the nature of substituents being either on the 4*H*-pyran or the adjacent rings.

Especially, among various chromene derivatives, 2-amino-4*H*-chromene with cyano-functionality has a potential applications in the treatment of rheumatoid, psoriasis, and cancer.[6] Other properties such as laser dyes,[7] optical brighteners,[8] fluorescence markers,[9] pigments,[10] cosmetics, and potent biodegradable agrochemicals[11] are well known for decades.

Due to the important aforementioned properties of chromene derivatives, considerable attention has been focused on the development of environmentally friendly methodologies to synthesize 2-amino-4*H*-chromene scaffold by cyclization of an aromatic/aliphatic aldehyde, malononitrile (or ethyl cyanoacetate), and diverse enolizable C–H activated acidic compounds. Malononitrile or ethyl cyanoacetate has been used as a nucleophile in organic syntheses.[12] A literature survey shows that several modified methods have been reported using different homogeneous or heterogeneous catalysts such as cetyltrimethylammonium chloride/bromide[13,14] tetrabutylammonium bromide,[15] triethylbenzylammonium chloride,[16] *N*,*N*-dimethylaminoethylbenzyldimethylammonium chloride,[17] chitosan,[18] KSF,[19] K_3PO_4,[20] K_2CO_3,[21] Na_2CO_3 under grinding,[22] nano-sized MgO,[23] heteropolyacid,[24] Mg/Al hydrotalcite,[25] $TiCl_4$,[26] methane sulfonic acid,[27] TMG-[bmim][x],[28] [BMIm]BF_4,[29] [2-aemim][PF_6],[30] DBU,[31] and piperidine under microwave irradiation.[32,33] However, many proposed methods for the

* Corresponding author. Tel.: +98 21 7724 0284; fax: +98 21 7749 1204; e-mail address: mdekamin@iust.ac.ir (M.G. Dekamin).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.11.068