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Original article

Nano structured spinel Co_3O_4-catalyzed four component reaction: a novel synthesis of Ugi adducts from aryl alcohols as a key reagent

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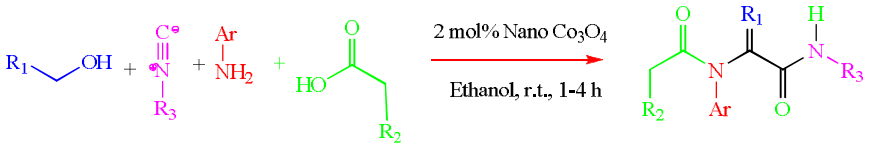
Graphical abstract



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ABSTRACT

A simple one pot procedure for the synthesis of α-amino acyl amide with chromone, indole, and napthalene substitution pattern is presented. This protocol involves the nano structured spinel Co_3O_4 catalysed coupling of aryl alcohols, anilines, carboxylic acids and *tert*-butyl isocyanide. The salient features of this protocol were simple procedure, mild reaction condition and high yield.

1. Introduction

Multicomponent synthesis has attracted the attention of organic chemists for assembling libraries of compounds in medicinal, combinatorial and heterocyclic chemistry. Many descriptive tags attached to MCRs are atom economy, automatable procedure, quick and simple implementation, high bond forming index, convergent, high selectivity, inherent exploratory power, time and energy saving and minimisation of chemical waste [1]. These features make MCRs well suited for the design and synthesis of diversified functional groups and heterocyclic scaffolds from readily available simple starting materials [2].

α-Amino acyl amides are important functional groups bearing excellent biological activities. For example, a wide variety of *α*-amino acyl amide derivatives has been used as agrochemical, pharmaceutical, biological agents. A large number of compounds bearing this group have entered preclinical and clinical trials for longer time. The pharmaceutical applications are represented by (Fig. 1) penicillin [3] (treatment for ear infection), cephalosporin [4] (treatment for skin and soft tissue infection), bicyclomycin [5] (treatment for diarrhoea), YH239-EE [6] (leukaemia treatment), nutlin-3a [7] (treatment for paediatric tumours and for haematological malignancies), TDP665759 [8] (cancer treatment) and xylocaine [9] (treatment for pain from scrapes, minor burns and insect bites). *α*-Amino acyl amide derivatives exhibit wide range of broad spectrum of biological activities such as anticancer [10,11], anaesthetics [12,13], antibiotics [14] and antibacterial [15] drugs. In the past few decades, many methods have been developed [16,17] for the synthesis of *α*-amino acyl amide derivatives. Among them, the classic approach involves: (i) from aldehyde, amine, isocyanide and phenol [18], (ii) from aldehyde, secondary amine, and isocyanide in aminoborane mediated and in the absence of acid [19], (iii) from aldehyde, amino acid and isocyanide [20,21], (iv) from *N*-aryl-1,2,3,4-tetrahydroisoquinoline, carboxylic acid and isonitrile [22], (v) from *γ*-keto acid, amine, and isocyanide [23], (vi) from aldehyde, amine, isocyanide and carboxylic acid [24,25].

The simplest and straight forward protocol was reported by Ugi involves the one pot four component condensation of aldehyde, ~~amine,~~ carboxylic acid and isocyanide. Unfortunately, this original procedure suffers from the long reaction duration, tedious

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