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Scientific paper

Photo-Oxidation Coupled Kabachnik–Fields and Bigenelli Reactions for Direct Conversion of Benzyl alcohols to α-Aminophosphonates and Dihydropyrimidones

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Abstract

A tandem one-pot solvent free approach for the direct conversion of benzyl alcohols to α-amino phosphonates and dihydropyrimidones is reported. The method relies on a metal free photo-oxidation of benzyl alcohols to benzaldehydes under UV irradiation using ammonium perchlorate followed by Kabachnik–Fields and Biginelli reactions. The reaction conditions are moderate and metal free with good substrate scope. The control experiments were performed to investigate the role of the ammonium perchlorate and molecular oxygen as oxidants. The quenching experiments in the presence of TEMPO and other radical quenchers suggest radical based mechanism.

Keywords: One-pot synthesis; photo-oxidation; benzyl alcohol; kabachnik–Fields reaction; biginelli reaction.

1. Introduction

The α-aminophosphonates are core structural components of many pharmacologically active molecules exhibiting diverse range of biological activities such as anticancer, HIV protease inhibitors, and serve as surrogates of α-amino acids.[1–3] The Pudovik reaction[4] and Kabachnik–Fields reactions[5] involving nucleophilic addition of phosphite to imines are the most widely used methods for the synthesis of α-aminophosphonates. The aminophosphonates can also be synthesised *via* acid-catalyzed (Lewis/Brønsted),[6,7] catalyst-free,[8] microwave assisted[9] condensation of H-phosphonates with aldehydes or imines. Furthermore, synthesis of α-aminophosphonates has also been achieved from substrates other than aldehydes using methylene aziridines,[10] dehydrogenative α-phosphonation of substituted *N*,*N*-dialkylanilines,[11] reduction of aryl nitro compounds,[12] reductive phosphination of amides,[13] and biomass-derived hydroxyl methyl furfural.[14] As such, we were particularly intrigued to explore the feasibility of ubiquitously available benzyl alcohols as substrates for the synthesis of α-aminophosphonates. To the best of our knowledge only report employing the use of benzyl alcohol has been carried out with an expensive gold supported catalyst.[15] Moreover, we wanted to examine if the benzyl alcohol could also serve as a surrogate of benzaldehydes for related reactions like Biginelli reaction leading to the formation of 1,4-dihydropyrimidones. Notably, 1,4-dihydropyrimidones are also a well known class of biologically active compounds with a range of therapeutic properties.[16] The traditional synthesis of dihydropyrimidones involves use of an aldehyde, a β-keto ester or β-diketone, and urea,[17] with most of the advances involving use of a Brønsted acid[18] or base,[19] metal based Lewis acids,[20] organocatalysts,[21] and heterogeneous catalysts.[22–25]

In this regard, photochemical reactions are undoubtedly greener alternatives to thermal processes, shifting the synthetic path of reaction from its solvo-thermal form to a neat and photochemical form; this has become a major step towards ecofriendly synthetic methodologies. The ap-