Novel multi-component syntheses of pyrimidines using β-CD in aqueous medium

Chowrasia Rakhi, Katla Ramesh, Mariana P. Darbem, Tabata A. Branquinho, Aline Rufino de Oliveira, Padma Sunitha Manjari, Nelson Luís C. Domingues

PII: S0040-4039(16)30212-X
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.02.106
Reference: TETL 47381

To appear in: *Tetrahedron Letters*

Received Date: 4 January 2016
Revised Date: 22 February 2016
Accepted Date: 26 February 2016

Please cite this article as: Rakhi, C., Ramesh, K., Darbem, M.P., Branquinho, T.A., Oliveira, A.R.d., Manjari, P.S., Domingues, N.L.C., Novel multi-component syntheses of pyrimidines using β-CD in aqueous medium, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.02.106

Novel multi-component syntheses of pyrimidines using β-CD in aqueous medium.

Chowrasia Rakhi,[a] Katla Ramesh,[b*] Mariana P. Darbem,[b] Tabata A. Branquinho,[b] Aline Rufino de Oliveira,[b] Padma Sunitha Manjari,[a*] and Nelson Luís C. Domingues.[b*]

[a]*Department of Chemistry, Osmania University, Hyderabad, Telangana State, India, 500004.* [b]*Organic Catalysis and Biocatalysis Laboratory OCBL/ FACET, Federal University of Grande Dourados—UFGD, Dourados/Itahúm rod. km 12 s/n, Zip Code 79804-970, Dourados, MS, Brazil.*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Aldehydes
Ammonium acetate
1,3-Dicarbonyl compounds
β-cyclodextrin
Pyrimidines
Water

ABSTRACT

Using β-cyclodextrin (β-CD) as a catalyst pyrimidine derivatives were synthesized for the first time in aqueous medium. β-CD is a recyclable, inexpensive, economically viable, non-toxic, and readily available material. Various aldehydes were used with ammonium acetate, and 1, 3-diketones to generate a series of pyrimidine derivatives in good to excellent yields. @ 2016 Elsevier Ltd. All rights reserved.

The strategy of multi-component reactions (MCRs) is considered a powerful tool in the field of organic, medicinal, and heterocyclic chemistry.[1] The main advantage of MCRs is the construction of numerous bonds in a single step within a short period of time by using three or more than three diverse substrates combined to develop a single product. MCRs is environmentally benign and atom efficient reactions which are very useful, and noteworthy, as well as cost-effective technique in the field of medicinal, and heterocyclic chemistry.[2]

Pyrimidine ring system occurs as a principal core skeleton among the drug scaffolds and also play crucial role as an important component in organic synthesis, and medicinal chemistry.[3] Pyrimidine derivatives gained prominence as they exhibit a wide range of biological and medicinal properties[4] such as antitumor, antibacterial, antifungal, anti-malarial and anticonvulsant.[5,6] Particularly 5-substituted pyrimidine nucleosides exhibit anti-mycobacterial activity.[7] Moreover, pyrimidine related compounds are also used in the treatment of hyperthyroidism, adult granulocytic leukemia, and acute leukemia in children.[8] These are also widely used in polymer, and supramolecular chemistry.[9] Some important representatives are shown in Figure. 1.

One such example is the microwave-assisted synthesis of aminopyrimidines from halopyrimidine and in phenylboronic acid in the presence of $Pd(PPh_3)_4$ and K_2CO_3 in toluene/ethanol developed by G. Luo and coworkers.[10]

Some of the important reports on pyrimidine derivatives such as microwave-assisted simple, one-pot, four-component synthesis of 2, 4, 6-triarylpyrimidines under solvent-free conditions from acetophenone, benzaldehyde, benzonitrile, hydroxylamine in the presence of acetic acid described by M. Adib and his co-authors.[11] Thomas J. J. Muller and his coworkers developed the synthesis of a novel three-component one-pot pyrimidine synthesis based upon coupling-isomerization sequence from 4-iodo nitrobenzene, 1-(3-thienyl)-propyn-1-ol, promoted by $Pd(PPh_3)_2Cl_2$, CuI, triethylamine, in THF.[12] Recently M. M. Heravi *et al*. reported a direct oxidative synthesis of pyrimidines using heteropolyacids, from 1, 3-diketone, NH_4OAc, and benzaldehyde.[13]

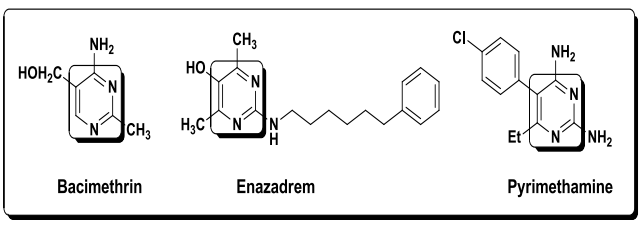

Figure 1. Some marketed drugs with pyrimidine skeleton.

*Corresponding author. Tel.: +55 (67) 3410 2081; fax: +55 (67) 3410 2072; e-mail: NelsonDomingues@ufgd.edu.br (Nelson Domingues), rameshkchem@gmail.com (Ramesh K), Psmanjari76@gmail.com (P. S. Manjari)