Efficient synthesis of diversely substituted pyrimidines by palladium catalyzed Suzuki-Miyaura coupling

Viral J. Faldu, Pratik K. Talpara, Viresh H. Shah

PII: S0040-4039(14)00075-6
DOI: http://dx.doi.org/10.1016/j.tetlet.2014.01.042
Reference: TETL 44074

To appear in: *Tetrahedron Letters*

Received Date: 20 November 2013
Revised Date: 10 January 2014
Accepted Date: 13 January 2014

Please cite this article as: Faldu, V.J., Talpara, P.K., Shah, V.H., Efficient synthesis of diversely substituted pyrimidines by palladium catalyzed Suzuki-Miyaura coupling, *Tetrahedron Letters* (2014), doi: http://dx.doi.org/10.1016/j.tetlet.2014.01.042

Efficient synthesis of diversely substituted pyrimidines by palladium catalyzed Suzuki-Miyaura coupling

Viral J. Faldu[a], Pratik K. Talpara[a], Viresh H. Shah[a]*

[a]*Department of Chemistry, Saurashtra University, Rajkot-360005.*

*Email: drvireshshah@gmail.com

Abstract- An efficient synthesis of 2-aryl/heteroaryl substituted pyrimidinyl ethanones **4(a-t)** was developed using a palladium-catalyzed Suzuki-Miyaura coupling reaction strategy. Use of $Pd(OAc)_2$ in presence of PPh_3 and Na_2CO_3 in 1,4-dioxane solvent was found to be the most effective reaction condition.

Keywords: Suzuki-Miyaura coupling, Palladium catalyst, Triphenylphosphine.

Palladium-catalyzed formation of carbon–carbon bonds have become an extremely powerful tool in modern synthetic organic chemistry.[1–4] In recent years, palladium-catalyzed Suzuki cross-coupling reactions have been increasingly employed for the construction of unsymmetrical biaryl units which have a wide range of applications in various areas such as pharmaceutical, herbicides, natural products.[5–10] The recent identification of a DHPM (dihydropyrimidine) analog as a potential new anticancer lead is involved in blocking mitosis by inhibition of a kinesin motor protein.[11]

The Suzuki reaction is an extremely powerful technique for the formation of biaryl compounds, consequently there has been significant attention focused on the development of catalysts that are able to promote the coupling of aryl halide substrates. Hence the development of catalysts for promoting Suzuki coupling of aryl halide substrates has attracted considerable interest. Suzuki-Miyaura coupling reactions are more efficient in organic media while employing $Pd(OAc)_2$, $Pd(PPh_3)_4$ and $PdCl_2$ as catalyst and among them use of $PdCl_2$ is found to be more efficient in the case of biphasic media.[12]

There are a number of drugs which possess pyrimidine derivatives, responsible for biological and therapeutic activities.[13] In view of the above, the present article reports an efficient regioselective approach for the synthesis of diversely substituted pyrimidinyl ethanones using Suzuki-Miyaura coupling. The effects of solvent, temperature and catalyst on the efficiency of the Suzuki-Miyaura coupling reaction have been studied.

The present work reports an efficient four-step approach for the synthesis of tetra substituted pyrimidinyl ethanones. The first step involves the Biginelli synthesis of 3,4-dihydropyrimidin-2(1H)-ones[14] **1(a-c)** followed by the oxidation with 60% nitric acid[15] to generate 2-oxo pyrimidinyl ethanones **2(a-c)**. The method in general provides moderate to good yields of oxidized products. However, factors such as steric hindrance, the presence of electron withdrawing substituents on phenyl ring and solubility of DHPMs (dihydropyrimidines) affect the yield and rate of reaction.