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New Synthesis of Imidazo[1,2-a]pyrimidines Catalysed by Gold Nanoparticles †

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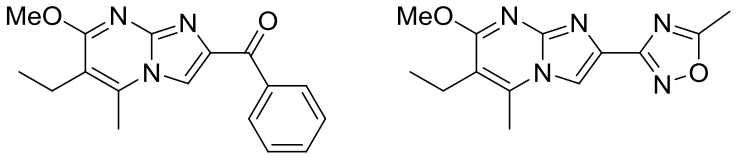
Abstract: Heterocyclic compounds are abundant in natural products, bioactive compounds and they play a huge role in the present repertoire of medicinal chemists due to their potential capability to modulate physicochemical properties. As a result, chemists have focused their efforts on the functionalization of heterocycles. Nitrogen containing fused heterocyclic compounds are important organic molecules. They are found in a variety of natural products, medicinal compounds and functional materials as structural fragments. The imidazo[1,2-a]pyrimidine skeleton is one of them, and it is linked to the pharmacological activity of related drugs. Anticancer activity medicines, anxiolytic drugs, and anti-inflammatory activity pharmaceuticals all have this structural pattern. Many of them have biological properties, antifungal, antimicrobial, antiviral, and anxiolytic properties, which are used in medications like divaplon and fasiplon. This invention of a new approach to manufacture 2-arylsubstituted imidazo[1,2-a]pyrimidines efficiently piqued our interest, given the powerful bioactivities of molecules with an imidazopyrimidine core. As a result, appropriate methods for manufacturing such molecules remain appealing. In this context, we would like to present a feasible green chemistry approach for the synthesis of 2-phenyl-imidazo[1,2-a]pyrimidines.

Keywords: imidazo[1,2-a]pyrimidine; efficient synthesis; catalyst; green chemistry.

1. Introduction

The synthesis of highly functionalized structures is of great interest in pharmaceutical science.[1]. Fused heterocyclic compounds are key structural scaffolds in a broad variety of natural products, drug molecules and functional materials[2]. Many imidazo[1,2-a]pyrimidine derivatives are significant as pharmaceuticals with several biological activities, and clinical examples such as fasiplon and divaplon (figure 1)[3, 4]. For those reasons, imidazo[1,2-a]pyrimidines are precious synthetic targets. Due to their high pharmacologic interest, there are a wide variety of synthetic protocols [5-8].



Divaplon Fasiplon

Figure 1: Structure of divaplon and fasiplon.

Recently, the use of catalysed organic chemistry methods has become a very powerful green chemical technology procedure from both the economical and synthetic points of view [8-11]. There is also another route to combine economic aspects with the environmental, that is, the use of green solvents [10, 11]. Here, we report a green, efficient, and rapid procedure for the synthesis of imidazo[1,2-a]pyrimidine derivatives (figure 2) obtained by different agents by using supported gold nanoparticles as the catalyst.

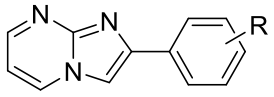
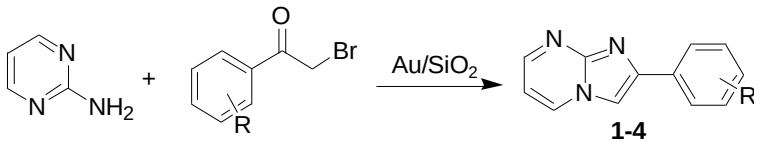


Figure 2: Structure of imidazo[1,2-a]pyrimidines

2. Results and Discussion

In conjugation with our recent research on the synthesis of nitrogen heterocycles, we describe here a novel and efficient procedure for the synthesis of fourimidazo[1,2-a]pyrimidine derivatives (scheme 1). We commenced our investigation with the reaction between 2-aminopyrimidine and 2-bromomophenacyl catalysed by gold nanoparticles under solvent free conditions (table1).



1-4

Scheme 1 Synthesis of imidazo[1,2-a]pyrimidines

Table 1. Optimization of conditions.

Entry	1	2	3	4
Solvent	neat	Ethanol	Methanol	Acetonitrile
Yield (%)	16	63	39	48

With optimized reaction conditions in hand, we set out to explore the scope of the reaction concerning different substituents on the bromoarylketone ring (Table 2).

Table 2. Synthesis of 2-arylimidazo[1,2-a]pyrimidine derivatives

Compound	1	2	3	4
R	H	4-Me	4-Br	4-OMe
Yield (%)	63	62	72	65
Ref.	[12-16]	[12-16]	[12, 14-16]	[12-15, 17]

3. Experimental Procedure

Herein, we describe a simple and efficient synthesis of imidazo[1,2-a]pyrimidines under green conditions using Au-SiO2 as a catalyst. The catalyst was prepared according to procedure [18-20].

General procedure: A mixture of bromoarylketone derivatives and 2-aminopyrimidine, was stirred under heating of green solvent and catalysed by gold nanoparticle. After cooling, the solid obtained was washed several times to give the desired products **1-4**.

4. Conclusions

We have developed a procedure to efficiently synthesize imidazo [1,2-a] pyrimidines through the reaction between arylketones and 2-aminopyrimidine under green conditions. The structure of the compound is confirmed by spectral analysis. The important characteristics of this protocol are mild reaction conditions, an environmentally friendly process and high yields that reflect the activity of the developed nanocatalyst. The environment friendliness and simplicity of this synthetic strategy will offer an attractive alternative to conventional methods.

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