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Solvent Free Green Synthesis of Amino Pyrimidines by using MgO-ZrO_2 as Versatile Catalyst

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Abstract: Due to the versatility in chemical and physical properties along with wide applications in the field of synthesis and technology, the mixed metal oxides (MMOs) secure their own position in heterogenous catalysis.
An efficient green synthesis of Amino Pyrimidines using MgO-ZrO_2 as heterogeneous catalyst is described. 2-acetylbenzofuran on treatment with substituted aldehydes under solvent free conditions affords the corresponding chalcones IIIa-e. The compounds IIIa-e on reaction with guanidine hydrochloride under microwave irradiation produce amino pyrimidines Va-e. This protocol has advantage of excellent yield, reusability, inexpensive and short reaction time at room temperature. The synthesized catalyst can be reused up to four consecutive cycles without any significant decrease in the yield.

Key Words: *Green Synthesis, Amino Pyrimidines, MMOs, Heterogeneous Catalyst*

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I. INTRODUCTION:

Nitrogen and oxygen containing heterocyclic compounds have received considerable attention due to their wide range of pharmacological activity. The pyrimidine derivatives have been reported to possess a variety of biological activity, notable among which are the analgesic[1], antihypertensive[2], antipyretic[3], antiviral[4] and anti-inflammatory activity[5]. These are also associated with nucleic acid, antibiotic, antimalarial and anticancer drugs[6]. Many of the pyrimidine derivatives are reported to possess potential CNS depressant properties[7]. Benzofuran derivatives, which are known to be present in many natural products[8], have physiological, pharma- cological and toxic properties and find application as sedatives, hypnotics[9], agrochemicals[10], pharma- ceuticals[11], cosmetics[12] and as the building blocks of optical brighteners[13]. Hence, there is continuing interest in their chemical synthesis. Cyclization reactions of various types have been used to produce substituted benzofurans[14]. The development of new synthetic approach is a challenge for the organic chemist. There are reports on the synthesis of pyrimidine derivatives by treating the chalcones with guanidine[15]. Hence, in the present paper is being reported a new and efficient method for the synthesis of substituted benzofuran derivatives containing pyrimidine ring at 2 position. This method is less time consuming and environmental friendly as compared to the existing conventional methods of synthesis. The synthesis of key starting material 2-acetyl- benzofuran **1** from salicyl aldehyde with chloroacetone in presence of KOH in ethanol was reported earlier[16]. The benzofuro-3-arylprop-2-en-1- ones **IIIa-e** were prepared by treating **1** with various aromatic aldehydes and NaOH in presence of MgO-ZrO_2 under solvent free conditions (**Scheme I**). **IIIa-e on further reaction with guanidine hydrochloride in presence of** MgO-ZrO_2 gives Amino pyrimidines **(Va-e)**.

Experimental

All commercially available chemicals and reagents were purchased from Aldrich and used without further purification. IR spectra were recorded on a Perkin-Elmer 1640 FT-IR instrument. The 1H- and 13C-NMR spectra were recorded on a Bruker DPX-300 NMR machine. Unless otherwise specified, CDCl3 was used as solvent. Mass spectra were recorded with a Bruker Daltonic Data Analysis 2.0 spectrometer.

Preparation of Mgo-ZrO_2 nano catalyst:

The ultradilution method have been used for the preparation of nano MgO-ZrO_2 as a continuation of our interest to explore the utility of this catalyst in organic synthesis. The methodology is explained below. In a typical experiment, for the preparation of MZ catalyst 3.10g of magnesium nitrate [Mg $(NO_3)_2.6H_2O$] and 8.11g zirconium oxychloride were dissolved together in 2 Litre flask with 1 Litre deionised water. The dropwise addition of dilute ammonia solution was made with vigorous stirring (RPM-5000) until the precipitation was complete. It take around 6-8 hours. During this task the constant pH=10 was maintained. The resultant precipitate was filtered and washed with distilled water till free from chloride ions. The residue was dried for 24 hrs at 383 K in an oven and the obtained precipitate of metal hydroxides heated in porecelain crucile progressively to 873 K for 10 hours.

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Synthesis of 1-(1-benzofuran-2-yl)-3-aryl- prop-2-en-1-one (IIIa-e)

A mixture of 2-acetylbenzofuran (0.01 mole, 1.60 g), aryl aldehyde (0.01 mole, 1.1 mL) and NaOH (0.01 mole, 0.4 g) were taken in a mortar and made a homogenous paste using a pestle. The paste was treated with various aldehydes in presence of $MgO\text{-}ZrO_2$ catalyst for 30 min. to 60 min. (depends on substituent on aldehyde) by using magnetic stirrer. After the completion of the reaction, the mixture was poured into ice cold water, extracted with chloroform, the organic layer dried over anhydrous sodium sulphate, concentrated under reduced pressure and the isolated solid purified by recrystallization from ethanol.

Synthesis of 6-(1-benzofuran-2-yl)-4-aryl-4, 5-dihydropyrimidin-2-amine (Va-e)

A paste of **IIIa-e** (0.01 mole, 2.93 g), guanidine hydrochloride (0.01 mole, 0.96 g) and NaOH (0.01 mole, 0.40 g) was magnetically stirred in presence of $MgO\text{-}ZrO_2$ catalyst for 5-20 min. (depends on substituent on aldehyde). Formed product is cooled and poured into ice cold water. The solid **Va-e**, which separated out was filtered off, washed with water, dried and purified by recrystallization from ethanol.

II. RESULTS AND DISCUSSION:

In order to explore our interest for the application of mixed metal oxide $MgO\text{-}ZrO_2$ in organic synthesis, we herein present a simple and efficient synthesis of Amino Pyrimidines **(Scheme 1 and Scheme 2)**.

The present protocol provide a variety of Amino Pyrimidines which are obtained in good to excellent yields (80-95%). According to this procedure, the reaction proceeded smoothly at room temperature to afford the corresponding Amino Pyrimidines in good yields. **(Table No.1 and Table No.2)**

Table 1: List of the synthesized chalcones*

Compound	R	Molecular Formula	Yield (%)	M.P.
2a	H	$C_{17}H_{12}O_2$	78	64
2b	NO_2	$C_{17}H_{11}NO_4$	80	72
2c	Cl	$C_{17}H_{11}ClO_2$	76	112
2d	CH_3	$C_{18}H_{14}O_2$	73	145
2e	OCH_3	$C_{18}H_{14}O_3$	75	70

***Reaction conditions:** 2-acetylbenzofuran (0.01 mole, 1.60 g), aryl aldehyde (0.01 mole, 1.1 mL) and NaOH (0.01 mole, 0.4 g), catalyst = 20 wt. % with respect to aldehyde, solvent free, temp. = 25°C.

Table 2: List of the synthesized amino pyrimidines*

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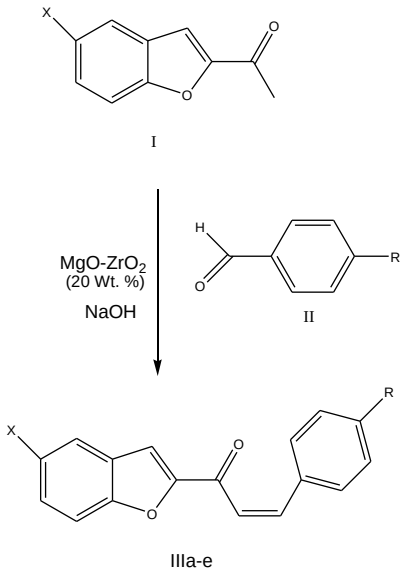
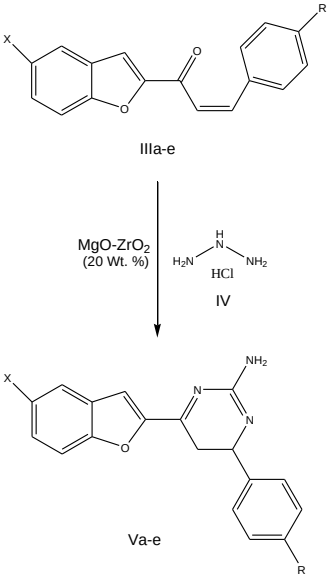
Compound	**R**	**Molecular Formula**	**Yield (%)**	**M.P.**
3a	**H**	**C18H15N3O**	**74**	**76**
3b	**NO2**	**C18H14N4O3**	**77**	**119**
3c	**Cl**	**C18H14ClN3O**	**71**	**154**
3d	**CH3**	**C19H17N3O**	**73**	**114**
3e	**OCH3**	**C19H17N3O2**	**72**	**102**

***Reaction conditions:** Aldehyde **IIIa-e** (0.01 mole, 2.93 g), guanidine hydrochloride (0.01 mole, 0.96 g) and NaOH (0.01 mole, 0.40 g),, catalyst = 20 wt. % with respect to aldehyde, solvent free, temp. = 25°C. All compounds are well characterized by spectroscopic techniques.



Scheme 1: synthesis of chalcones



Scheme 2: synthesis of Amino Pyrimidines from chalcones

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III. CONCLUSION:

In conclusion, we have reported an efficient two step procedure for the synthesis of amino pyrimidines using mix metal oxide MgO-ZrO_2 as catalyst. The major advantage of this method is the ease of work-up. This method also offers some other merits such as clean synthesis, high yields of products, shorter reaction times and use of various substrates, which make it useful and attractive strategy for the synthesis of amino pyrimidines.

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