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NOTE

Solid State Synthesis of 4-Aryl-3,4-dihydropyrimidine-2-(1*H*)-ones

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An efficient, solid state, microwave assisted synthesis of 4-aryl-3,4-dihydropyrimidine-2-(1*H*)-ones using zeolite 4A is reported in Biginelli, onepot, three component coupling reaction of 1,3-diketones, aldehydes and urea.

Key Words: Solid state synthesis, Multi component one-pot reaction, 4-aryl-3,4-dihydropyrimidine-2(1*H*)-ones, Microwave.

Biginelli reaction is a multi component reaction for the synthesis of dihydropyrimidinones, which involved one pot condensation of ethyl acetoacetate, benzaldehyde and urea under acidic conditions. This method involves longer reaction time,harsh reaction conditions and low yields. Therefore there is a need for the alternative route for the synthesis of 4-aryl-3,4-dihydropyrimidine-2-(1*H*)-ones (DHPMs). The Biginelli reaction was reported more than a century ago and recently reviewed[1,2]. There are several reports in the literature for the synthesis of DHPMs[3-13]. There are some drawbacks in many of these methods due to the usage of expensive reagents, reaction conditions, longer reaction time, yields, *etc*. DHPMs have wide range of biological activities[1,2,14]. Apart from the synthetic DHPM derivatives, several marine natural products with interesting biological activities containing the dihydropyrimidine-5-carboxylate core have recently been isolated[15]. Most notably among these, batzalladine alkaloids A and B are found to be potent HIV-gp-120-CD4 inhibitors[16].

Microwave assisted solid state reactions are already known for high yields, specificity and shorter reaction time and also environment friendly[17-19]. Literature shows that zeolites are used as inorganic solid acid catalyst for organic synthesis[20-23]. Knowing the biological importance of the DHPMs and need of the alternative procedure, it has been planned to carry out the synthesis of DHPMs using inorganic solid catalyst zeolite 4A (a cheaper one) under, microwave assisted, solid state conditions. To the best of our knowledge this is the first report using zeolite 4A for the synthesis of dihydropyrimidinones in solid state under microwave irradiation.

A thoroughly mixed mixture of benzaldehyde (20 mmol), ethyl acetoacetate (20 mmol), urea (20 mmol) and sufficient amount of zeolite 4A were irradiated

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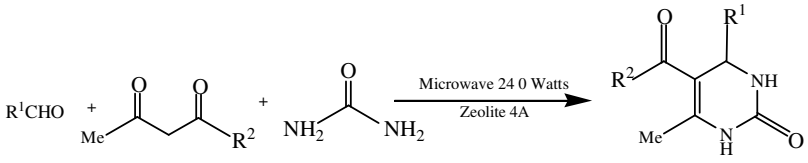
inside a microwave oven. After the reaction was complete the reaction mixture was cool down. The product was recovered from the zeolite with the help of Soxhelt using alcohol as solvent. Finally the product was recrystallized from the alcohol.

1,3-Diketone, urea and aldehyde were mixed with zeolite and irradiated in a microwave oven. Results are presented in Table-1 and **Scheme-I**.

TABLE-1

Product	R^1	R^2	Time (min)	Yield (%)	m.p. (ºC)
1	Ph	OEt	1.5	98	202
2	4-(NO_2)-C_6H_4	OEt	2.0	96	206-208
3	4-(OMe) -C_6H_4	OEt	3.0	94	203
4	3-(NO_2)-C_6H_4	OEt	3.0	92	226
5	2-(Cl)-C_6H_4	OEt	2.0	94	214
6	4-(Cl)-C_6H_4	OEt	2.5	95	211
7	Furyl	OEt	3.5	82	201
8	Ph	OMe	2.0	98	210
9	4-(NO_2)-C_6H_4	OMe	2.0	93	236

All the compounds prepared were known compounds.



Scheme-I

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