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SIO_2.CAA: AN EFFICIENT CATALYST FOR ONE POT SYNTHESIS OF 4,6-DIARYLPYRIMIDINE- 2(1H)-ONES OR THIONES

Vishvanath Dhamba Patil*, Prathamesh Vidyadhar Gidh, Amruta Mohan Salve

Organic Chemistry Research Laboratory, Department of Chemistry, C.K.Thakur A.C.S. College New Panvel, Raigad, Maharashtra, India-410206.

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ABSTRACT

An efficient method for the synthesis of 4,6-diarylpyrimidin-2(1H)-ones or thiones by using SiO_2.CAA. The condensation of acetophenone, aldehydes and urea or thiourea in the presence of silica supported catalyst was employed to synthesize a variety of pyrimidinones or thiones in excellent yields. The remarkable feature of this synthetic pathway is simple workup, shorter reaction times, high yields

Corresponding author
Vishvanath Dhamba Patil
Organic Chemistry Research Laboratory,
Department of Chemistry,
C.K.Thakur A.C.S. College New Panvel,
Raigad, Maharashtra, India-410206
vishvanathpatil@gmail.com

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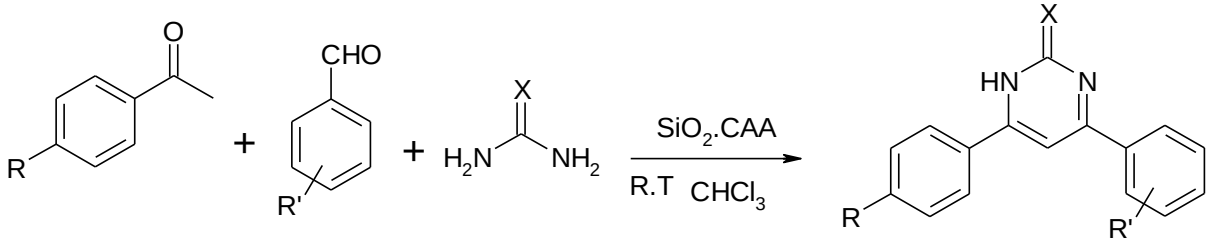
INTRODUCTION

SiO_2.CAA is an efficient catalyst for synthesis of 4,6-diarylpyrimidin-2(1H)-ones or thiones. The development of simple, efficient and economically viable chemical process or methodologies for widely used organic compounds is in great demand. Silica supported Chloro acetic acid (SiO_2.CAA) is an efficient catalyst for synthesis of 4,6-diarylpyrimidin-2(1H)-ones or thiones. Pyrimidines and their derivatives are pharmacologically important compounds with broad biological activity, including antiviral, antibacterial, antitumor and antihypertensive agents antagonists, calcium-channel blockers[1].

Recently, pyrimidinones have been considered as a compound for the development of anticancer drugs [2, 3]. The efficient approach for the synthesis pyrimidinones reported by Biginelli involves a multi-component reaction (MCRs) [4], but this Biginelli-type reactions has different disadvantages such as harsh conditions, long reaction times, low yields.

Multi-component synthetic procedures [5-8] for the preparation of pyrimidinones. These include assistance of microwave [9, 10] or ultrasound irradiation[11, 12] and use of Lewis and/or Bronsted acids as catalysts, $FeCl_3$-supported nanopore silica [10], ferric perchlorate [13], polyoxomethalate [14], strontium(II) nitrate [15], cerium(III) chloride [16], ytterbium chloride [17], heteropoly acids [18], L-proline [19], silica sulfuric acid [20] have been used.

In these communication, we would like to report a method for the synthesis 4,6-diarylpyrimidin-2(1H)-ones or thiones which is simple, mild, involving use of cost effective and efficient catalyst. Synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones using silica supported CAA catalyst (Scheme 1).



X= O or S

EXPERIMENTAL SECTION

All chemical were obtained from Sigma-Aldrich, Merck and used without purification. Open capillary method involving use of Thiels tube was used to determine melting points. IR spectra were recorded with Perkin-Elmer FTIR spectrometer as KBr pellets. H^1NMR spectra were acquired on a 400 MHz Varian FT-NMR spectrometer. The chemical shift values were expressed in δ with reference to tetra methyl silane (TMS) as an internal standard. The progress of reaction was monitored using TLC (Silica gel 200-475 mesh, a mixture of Pet ether and ethyl acetate in 9:1 proportion as solvent system) and the product were purified by recrystallization from suitable solvent. The synthesized 4,6-diarylpyrimidin-2(1*H*)-ones or thiones were known compound.

General procedure for the synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones or thiones:

A mixture of Acetophenone (1 mmol), aldehyde (1 mmol), Urea/ Thiourea (1 mmol) was stirred magnetically in the presence of SiO_2.CAA (0.1mmol) Chloroform(1ml) at room temperature. The progress of the reaction was monitored by thin-layer chromatography. The completion of reaction confirmed with TLC. The product was dried over anhydrous Na_2SO_4 and then evaporated under vacuum to afford the crude product which on further purification by column chromatography. In all the cases, the product obtained after the usual work up gave satisfactory spectral data.

Spectral characterisition of selected 4,6-diarylpyrimidin-2(1*H*)-ones

4, 6-Diphenyl-pyrimidin-2(1H)-one [1c]
IR (KBr) ν_{max} = 3356, 3158, 2962, 1615, 1504 cm^{-1};
^{1}HN-MR (DMSO, 300 MHz): δ_H =7.58 − 7.67 (m, 7H, H-5 and H_{Ar}), 8.12–8.20 (m, 4H, H_{Ar}) ppm.4-(*p*-Methyl-phenyl)-6-phenyl-pyrimidin-2(1H)-one [6c]
IR (KBr) ν_{max} =3449, 3099, 2923, 1620, 1513, 1460 cm^{-1};
^{1}HNMR (DMSO, 300 MHz): δ_H =2.36 (s, 3H, CH_3), 7.35 (d, 2H, J =7.5, H_{Ar}), 7.55– 7.59 (m, 4H, H-5 and H_{Ar}), 8.05 (d, 2H, J =7.6 Hz, H_{Ar}), 8.12 (d, 2H, J =5.75, H_{Ar}) ppm.

RESULTS AND DISCUSSION

The catalytic activity of SiO_2.CAA for the synthesis of 4,6-diarylpyrimidin-2(1H)-ones or thiones obtained from Acetophenone (1 mmol), Aldehyde (1 mmol), Urea/ Thiourea (1 mmol) under room temperature was studied and it was found that the application of less than 0.1 mmol of SiO_2.CAA in chloroform (5ml) gave moderate yield of the corresponding 4,6-diarylpyrimidin-2(1H)-ones (Table 1, entries 1-12), whereas the use of more than 0.1 mmol gave an moderated yield(Table 1, entries 10-12).

It was treated with 1mmol of acetophenone , 1mmol of aldehyde, 1mmol of urea/thiourea in presence of 0.1 mmol of SiO_2. CAA in various solvents at room temperature (Table 1). The reaction in THF, CH_2Cl_2, Et_2O, EtOAc, DMF (Table 1, entries 1-7) were found less effective. Since then, we have carried out the reaction in the presence of the $CHCl_3$ solvent to get an excellent yield (92%, entries 7 and 8).

Table- 1.: Catalytic effect of SiO_2.CAA in reaction with acetophenone, aldehyde and urea/ thiourea in presence of SiO_2.CAA with different solvents at room temperature.

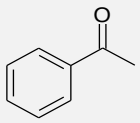
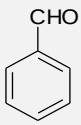
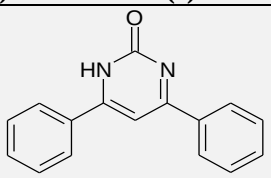
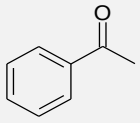
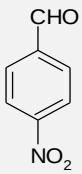
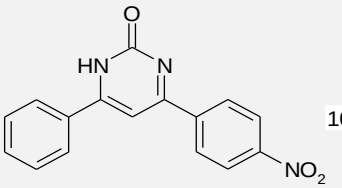
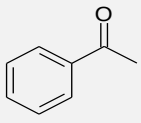
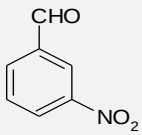
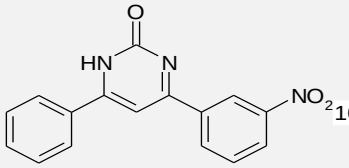
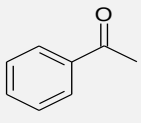
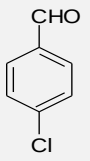
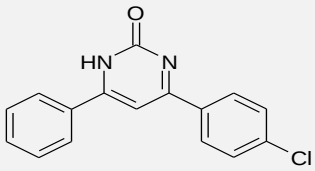
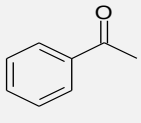
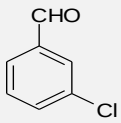
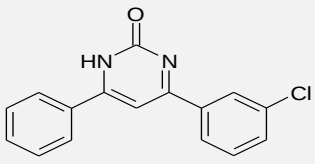
Entry	Solvent	SiO2CAA (mmol)	Time(min)	Yield[a](%)
1	Neat	-	120	5
2	THF	0.1	60	40
3	CH_3CN	0.1	60	72
4	CH_2Cl_2	0.1	60	60
5	Et_2O	0.1	90	75
6	EtOAc	0.1	10	80
7	DMF	0.1	10	85
8	$CHCl_3$	0.01	10	70
9	$CHCl_3$	0.05	10	90
10	**$CHCl_3$**	**0.1(15mg)**	**10**	**92**
11	$CHCl_3$	0.1	10	92
12	$CHCl_3$	0.15	10	92

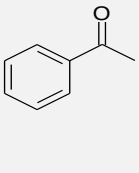
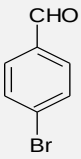
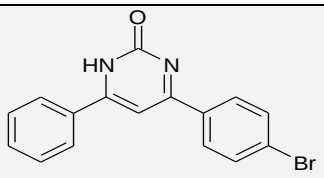
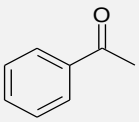
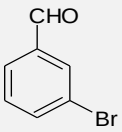
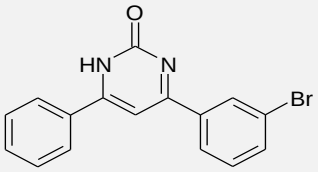
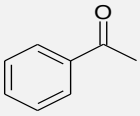
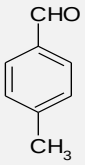
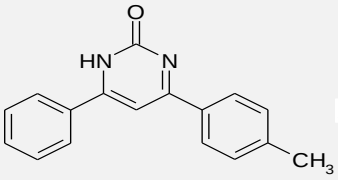
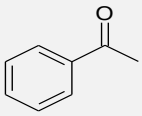
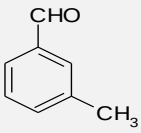
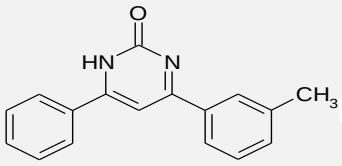
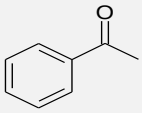
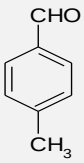
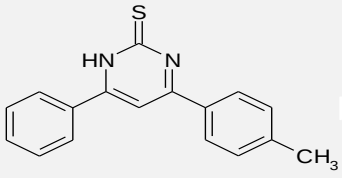
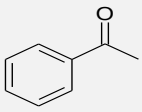
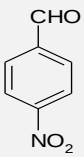
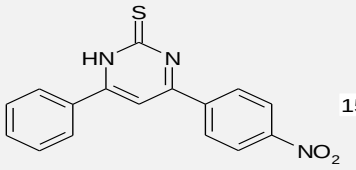
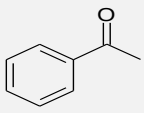
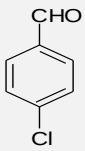
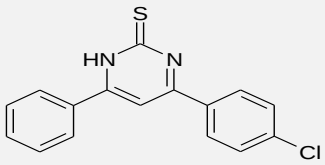
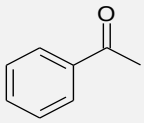
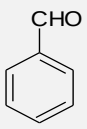
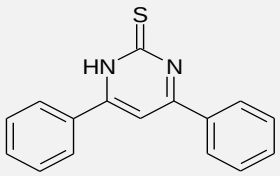
[a] Isolated yields of corresponding products.

As summarized in Table 2, aromatic aldehydes with electron-donating or electon withdrawing groups, with various aldehydes, acetophenone and urea/thiourea in presence of SiO_2.CAA were reacted, resulting in corresponding 4,6-diarylpyrimidin-2(1H)-ones or thiones in good to excellent yields.

A broad range of structurally diverse aromatic aldehydes have been used in this condensation. (Table-2, entries 1-13). We found that electron donating group gives excellent yields (Table-2, entries 4-10,12). or withdrawing group (Table-2, entries 2,3,11). on aromatic aldehydes gave moderated yields. Therefore the method can be used for wide range of reactants with different functional group.

Table- 2.: Reaction with acetophenone, aldehyde and urea/thiourea in presence of SiO_2.CAA at room temperature.

Entry	Acetophenone	Aldehyde(a)	X(b)	Product(c)	Time(min)	Yield[d](%)
1.			O		10	94
2.			O		10	90
3.			O		10	89
4.			O		10	92
5.			O		10	90

6.			O		10	91
7.			O		10	90
8.			O		15	89
9.			O		10	90
10.			S		15	87
11.			S		15	88
12.			S		15	86
13.			S		15	92

[a,b] The substrates were treated with acetophenone (1 mmol) by stirring at room temperature with SiO_2.CAA in presence of chloroform as solvent.
[c] All products were identified by their IR and ^1H NMR spectra
[d] Isolated yields after column chromatography.

CONCLUSION

In conclusion, we have reported a simple and new catalytic method for the synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones or thiones by one-pot three-component reaction of acetophenone, aromatic aldehydes, and urea/thiourea using SiO_2.CAA.. High yields, relatively short reaction times and easy workup are few of the advantages of this procedure. On the basis of data for reaction time and yield, silica supported chloro acetic acid was found to be more efficient materials as catalyst in synthesis. Silica supported chloro acetic acid would be useful in synthesis of other biologically active heterocycles through multicomponent reaction pathway.

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