



Research Article

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SiO₂.CAA: An Efficient Catalyst for One Pot Synthesis of 4,6-Diarylpyrimidin-2(1H)-Ones or Thiones

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ABSTRACT

An efficient method for the synthesis of 4,6-diarylpyrimidin-2(1H)-ones or thiones by using SiO₂.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 are simple workup, shorter reaction times, high yields.

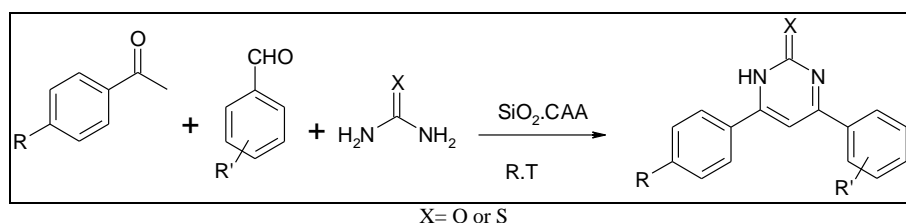
Keywords: 4,6-diarylpyrimidin-2(1H)-ones; Urea; Thiourea; Aldehydes; SiO₂.CAA

INTRODUCTION

Silica supported Chloro acetic acid(SiO₂.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 are in great demand. Silica supported Chloro acetic acid 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 Brønsted acids as catalysts, FeCl₃-supported nanopore silica [10], ferric perchlorate [13], polyoxometalate [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(1H)-ones using silica supported CAA catalyst (Scheme 1).



EXPERIMENTAL SECTION

All chemical were obtained from Sigma-Aldrich, Merck and used without purification. Open capillary method involving use of Thiele tube was used to determine melting points. IR spectra were recorded with Perkin-Elmer FTIR spectrometer as KBr pellets. HNMR 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(1H)-ones or thiones were known compound.

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

A mixture of Acetophenone (1 mmol), aldehyde (1 mmol), Urea/Thiourea (1 mmol) was stirred magnetically in the presence of SiO₂.CAA (0.1mmol to 15mg) Chloroform(1ml) at room temperature. The progress of the reaction was monitored by thin-layer chromatography. The completion of reaction conformed with TLC. The product was dried over anhydrous Na₂SO₄ 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 characterisation of selected 4,6-diarylpyrimidin-2(1H)-ones

1. 4,6-Diphenyl-pyrimidin-2(1H)-one [1c]

IR (KBr) ν_{\max} = 3356, 3158, 2962, 1615, 1504 cm⁻¹;

¹H-NMR (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.

2. 4-(*p*-Methyl-phenyl)-6-phenyl-pyrimidin-2(1H)-one [6c]

IR (KBr) ν_{\max} = 3449, 3099, 2923, 1620, 1513, 1460 cm⁻¹;

¹H-NMR (DMSO, 300 MHz): δ_{H} = 2.36 (s, 3H, CH₃), 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 SiO₂.CAA for the 4,6-diarylpyrimidin-2(1H)-ones or thiones with 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 SiO₂.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 SiO₂.CAA in various solvents at room temperature (Table 1). The reaction in THF, CH₂Cl₂, Et₂O, EtOAc, DMF (Table 1, entries 1-7) were found less effective. Since then, we have carried out the reaction in the presence of the CHCl₃ solvent to get an excellent yield (92%, entries 7 and 8).

Table 1: Catalytic effect of SiO₂.CAA in reaction with acetophenone, aldehyde and urea/ thiourea in presence of SiO₂.CAA with different solvents at room temperature

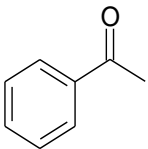
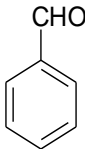
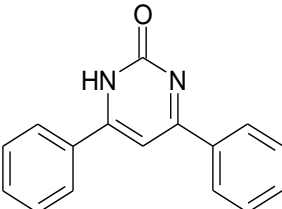
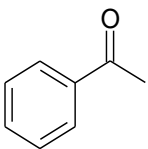
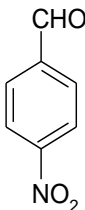
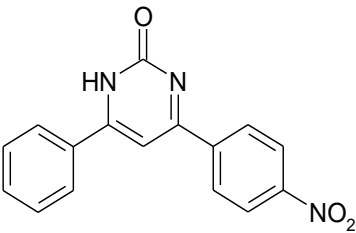
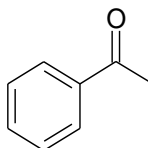
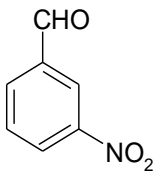
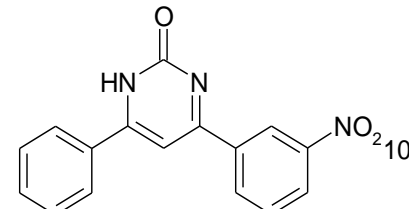
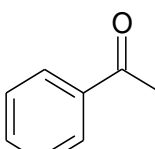
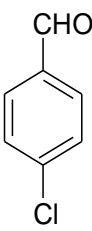
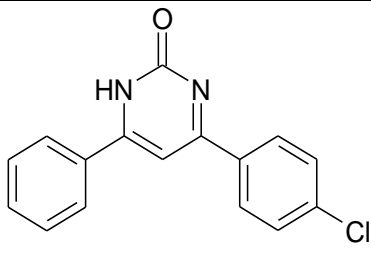
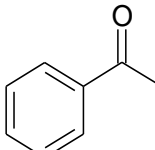
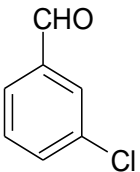
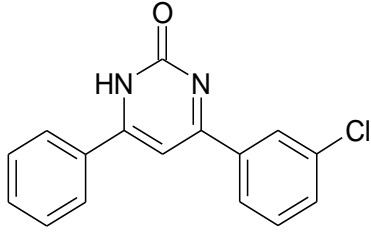
Entry	Solvent	SiO ₂ .CAA (mmol)	Time(min)	Yield ^a (%)
1	Neat	-	120	5
2	THF	0.1	60	40
3	CH ₃ CN	0.1	60	72
4	CH ₂ Cl ₂	0.1	60	60
5	Et ₂ O	0.1	90	75
6	EtOAc	0.1	10	80
7	DMF	0.1	10	85
8	CHCl ₃	0.01	10	70
9	CHCl ₃	0.05	10	90
10	CHCl ₃	0.1(15mg)	10	92
11	CHCl ₃	0.1	10	92
12	CHCl ₃	0.15	10	92

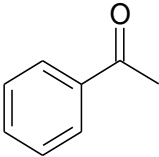
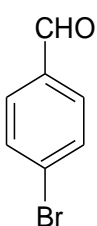
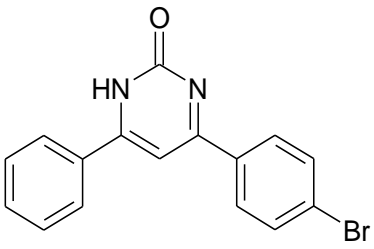
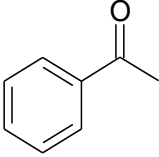
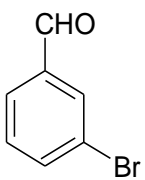
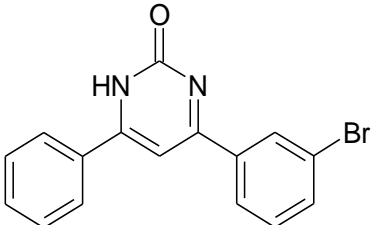
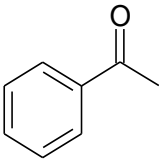
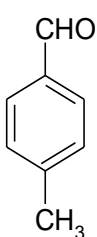
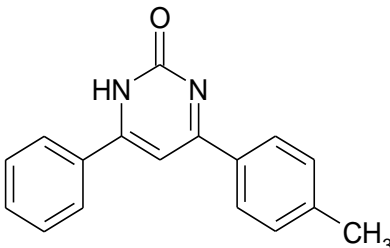
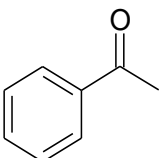
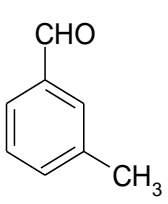
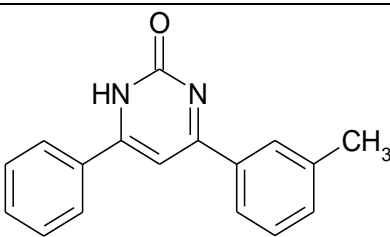
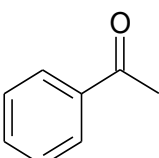
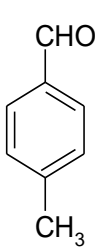
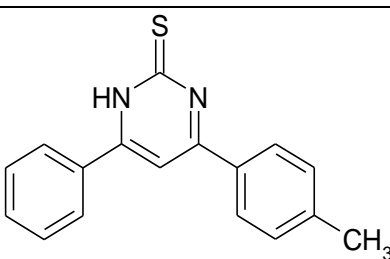
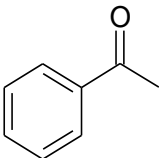
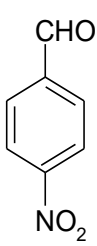
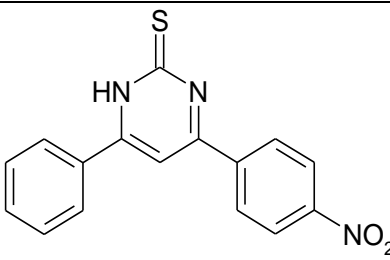
^aIsolated yields of corresponding products

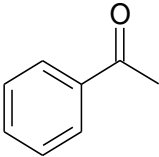
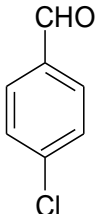
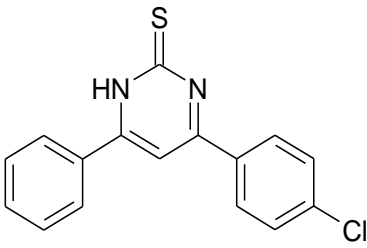
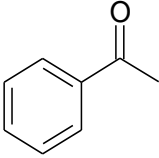
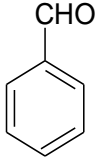
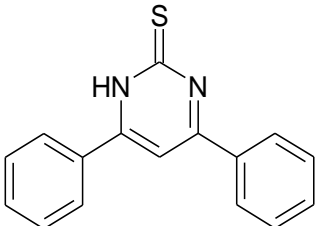
As summarized in Table 2, aromatic aldehydes with electron-donating or electron withdrawing groups, with various aldehydes, acetophenone and urea/thiourea in presence of SiO₂.CAA were reacted, resulting in corresponding 4,6-diarylpyrimidin-2(1H)-ones or thiones in good to excellent yields.

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 SiO₂.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 SiO₂.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(1H)-ones or thiones by one-pot three-component reaction of acetophenone, aromatic aldehydes, and urea/thiourea using SiO₂.CAA. High yields, relatively short reaction times and easy workup are few of the advantages of this procedure.

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