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One Pot Synthesis of 1, 5-Benzothiazepines Using SnO2/SiO2 Nanocomposite Catalyst

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ABSTRACT

SnO2/SiO2 catalyzed synthesis of 1,5-benzothiazepines by the condensation of chalcone and o-aminothiophenol in presence of ethanol as solvent. The synthesis highlights a synthesis and use of SnO2/SiO2 nanocomposite heterogeneous catalyst and its reusability. The method is cost effective and ecofriendly. And use of ethanol as a solvent makes the method more green and efficient. The method has simple workup procedure and the products are obtained in good to moderate yields.

Keywords : 1, 5-benzothiazepines, chalcone, o-aminothiophenol, SnO2/SiO2 nanocomposite.

I. INTRODUCTION

The 1,5-benzothiazepines are very versatile and are present in number of famous drugs.1,5-benzothiazepines are being used as antidepressants, calcium antagonists and coronary Vasodilators. The 1,5-benzothiazepine is a honored class of pharamacophore, as compounds having this structural component possess a large range of biological activities like squalene synthetase inhibitor [1], anticonvulsant, anti-anginal [2,3], anti HIV [4],V2 arginine [5], Ca+2 channel antagonist vasopressin receptor antagonist [6], HIV-1 reverse transcriptase inhibitor [7,9] etc. Thus there is need to develop novel methodologies for the synthesis of 1,5 benzothiazepines.

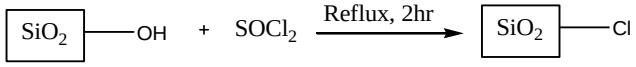
A mild, general method still remains a challenge. Thus to overcome the challenge the use of easily available, reusable solid acid catalyst, silica chloride there are many application of solid supported catalyst as safety in handling, rate enhancement and easy workup procedures [10 -12]. In continuation to our previous work on ultrasound irradiated synthesis which is important technique in synthetic organic chemistry. It has been used as an important energy source for the organic reactions. Simple experimental

procedure, increased selectivity, very high yields, and clean reaction [13 -15].

II. EXPERIMENTAL SECTION

Procedure for Optimization of reaction conditions for the synthesis of 1,5-benzothiazepines.

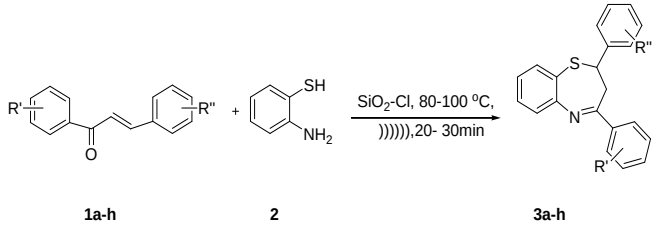
The model reaction between chalcone **1d** (1.0 mmol) and o-aminothiophenol **2d** (1.2 mmol) (Scheme). The reaction which is condensation reaction catalyzed by silica chloride (SiO_2-Cl) and optimization using different mol percentage for the reaction which was carried out under ultrasound irradiation. The results obtained are summarized in **Table 1**.Using (SiO_2-Cl) (15 mol %) (entry 10) with solvent free conditions at 80 - 100 °C for 30 min gave excellent yield as compared to other. And for our further synthesis of all other 1,5-benzothiazepines derivatives we have chosen (SiO_2-Cl) (15 mol %) at solvent free under ultrasound irradiation.



Scheme 1: Synthesis of silica chloride

Procedure for the synthesis 1,5-benzothiazepines (3a-h).

A mixture of chalcone **1d** (1.0 mmol) and o-aminothiophenol **2d** (1.2 mmol) to that (SiO_2-Cl) (15 mol %) was added and the reaction mixture was kept in the ultrasonic bath and was irradiated at 80- 100°C for about 20-30 min. (the progress of reaction was monitored by TLC) separately as indicated in (**Table 2**). After the reaction was completed the reaction mass was poured on crushed ice. The obtained solid was filtered, washed with water and dried. The crude compound was crystallized using DMF-Ethanol.



Scheme 2. Synthesis of 1,5-benzothiazepines from chalcones and o-aminothiophenol.

Table 1: Optimization of reaction conditions for the synthesis of 1,5-benzothiazepines using ultrasound irradiation.

Entry	Catalyst/ mol (%)	Solvent	Time (min)	Yield[a] (%)
1	-	EtOH	90	5[b]
2	SiO_2-Cl (5)	THF	70	40
3	SiO_2-Cl (10)	THF	70	55
4	SiO_2-Cl (5)	MeCN	70	50
5	SiO_2-Cl (10)	MeCN	70	53
6	SiO_2-Cl (5)	Toluene	60	40
7	SiO_2-Cl (10)	Toluene	60	48
8	SiO_2-Cl (5)	-	40	60
9	SiO_2-Cl (10)	-	25	78
10	SiO_2-Cl (15)	-	25	94

[a]Isolated yields. [b]Not completed

Spectral data for representative compound 3c.

Compound 3c**:** IR (KBr): 3418, 2860, 1610, 1535, 1502, 835 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 3H, CH_3), 3.02 (apparent triplet, J = 12Hz, 1H, C_3-H), 3.27 (dd, J = 12.4 Hz & 4.3 Hz, 1H, C_3-H), 5.05 (dd, J = 11.5 Hz & 4.5 Hz, 1H, C_2-H), 6.89-7.03 (m, 3H, Ar-H), 7.15-7.26 (m, 1H, Ar-H),7.27-7.32 (m, 3H, Ar-H), 7.43-7.52 (m, 2H, Ar-H), 7.63 (d, J = 7.3 Hz, 1H, Ar-H); MS (M+): m/z 396.5.

Table 2. One pot Synthesis of 1,5-benzothiazepines (**3a-h**) using PEG-400.

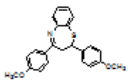
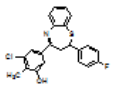
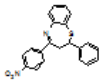
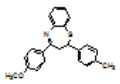
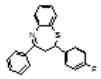
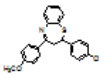
Comp.	Product	m.p °C	Ultrasound Method	
			Time (min)	Yield (%)
3a		107 -109	25	92
3b		112 -116	25	93
3c		173 - 176	30	90
3d		116 - 118	30	92
3e		110 - 112	35	88
3f		101 - 103	35	92
3g		124-127	30	86
3h		133 - 135	30	88

Table 3 : Recyclability and reusability of catalyst SiO_2-Cl.

Number of Runs	Yield (%)[a]	Catalyst recovery (%)[b]
1	93	96
2	91	94
3	88	91
4	87	89

[a]Isolated yields.

[b]SiO_2-Cl was recovered and for number of runs.

III. RESULT AND DISCUSSION

One pot cyclocondensation of chalcone **1d** (1.0 mmol) and o-aminothiophenol **2d** (1.2 mmol) to that (SiO_2-Cl) (15 mol %) was added it was carried out under ultrasound irradiation which result into the subsequent 1,5-benzothiazepines (**3a-h**) as given in (**Table 2**). We have screened various percentage silica chloride (SiO_2-Cl) and optimization using different mol percentage for the reaction which was carried out under ultrasound irradiation. The results obtained are summarized in **Table 1**.

Here good yields was obtained for (SiO_2-Cl) (15 mol %) (entry 10) with ethanol as solvent at 80 - 100 °C for 30 min. And thus the reaction was optimized and the method was used for further synthesis derivatives and the results obtained are given in **Table 2**. All the reaction (**3a-h**) is repeated with recovery of catalyst for three to four times the loss of catalyst was 2-3 % with good yield which is appreciable **Table 3**.

IV. CONCLUSION

In conclusion, we have developed a simple and highly efficient method were 1,5-benzothiazepines and their derivatives are synthesized using silica chloride (SiO_2-Cl) as heterogeneous catalyst which is reusable and cost-effective. The reaction is performed in ethanol as solvent under ultrasound irradiation. Thus the method is clean and efficient method. Further studies on the biological activities of the products and application of this methodology to other interesting benzothiazepines derivatives are underway in our laboratory.

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