# Plant Assisted Zinc Oxide Nano-Particles for Synthesis of 1, 5-Benzothiazepines

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***Abstract***

*One step synthesis of various aromatic substituted, 5-benzothiazepines Carried by the reaction of different substituted chalcone with ortho-aminothiophenol in sonication at room temperature using plant assisted zinc oxide nanoparticles. This reaction method is very mild reaction condition, very short reaction time as compared to the other conventional methods. The structural assignment of the final product has been done by spectral techniques.*

**Keywords** - *different substituted chalcone, ortho-aminothiophenol, short reaction time*

## I. INTRODUCTION

The 1, 5-benzothiazepines is most important in great number of well known drugs. Now a day's 1,5-benzothiazepines are being used as calcium antagonists and coronary vasodilators, as antidepressants. The 1,5-benzothiazepine moiety is important class of pharmacophore, as compounds bearing this structural unit possess very broad spectrum of biological activities such as anti-convulsant,1 $Ca^{+2}$ channel antagonist,2 anti-anginal,3 anti HIV,4 1,5 antimicrobial [5],antifungal [6],antihypertensive [7], anticancer [8], antiarrhythmic [9], anti-inflammatory [10], coronary vasodilatory [11], anticonvulsant [12], CNS depressant [13], anti-HIV [14] etc. Number of different methods have been reported for the synthesis of 1, 5-benzothiazepines [15].Very common used method involves the reaction of 2-aminobenzenethiol with α, β-unsaturated carbonyl compounds i.e. ketones or chalcones by different methods. Due to very broad profile of biological activities and availability of different routes for synthesis of 1, 5-benzothiazepines, there is huge scope for the synthesis of 1, 5-benzothiazepines and derivatives.

The very common strategy for the preparation of the 1,5- benzothiazepines moiety is the reaction of chalcones with o-aminothiophenol .The various reported methodologies involve the use of inorganic solid supports such as alumina, silica gel and clay under microwave irradiation, acetic acid or TFA, HCl,[15] piperidine.[17] In most of the cases affords the uncyclized thia-Michael adduct as the final product and the 1,5-benzothiazepines are formed only in the case of activated (methoxy or methyl substituted) bis2-aminophenyldisulfides. Many of these processes suffer from limitations such as requiring harsh conditions, highly expensive reagents, very high catalyst loading, highly corrosive reagents, or very toxic ions; low yields and occurrence of several side reactions. It is also necessary to find a very milder, selective, nonhazardous and inexpensive reagent and there is necessity to develop a more effective synthetic procedure for the synthesis of 1, 5-benzothiazepines.

Ultrasound accelerated chemical reactions are well known and proceed via the formation and adiabatic collapse of transient cavitations bubbles during the sonication process. Ultrasound irradiation has been demonstrated as an alternative energy source for organic reactions ordinarily accomplished by heating at high temperature many homogeneous and heterogeneous reactions can be conducted smoothly by sonication to provide improved yields and increased selectivity's. We have used plant assisted zinc oxide nanoparticles during synthesis using sonication approach.

## II. MATERIALS AND METHODS

Reactions were carried out under air and nitrogen atmosphere in dried glass-ware and assembly. Infrared spectra were recorded using scimanzdu spectrometer. $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on a Brucker AC (300 MHz for $^{1}H$ NMR and 300 MHz for $^{13}C$ NMR) spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded using Perkin Elmer SQ 300 vector model. Melting points were determined using capillary method .Precoated aluminium sheets (silica gel 60 F254, Merck) were used for thin-layer chromatography (TLC) and spots were visualized under UV light. All other chemicals were obtained from local chemical suppliers and were used without further purification.

## III. GENERAL METHOD FOR SYNTHESIS ZINC OXIDE PLANT ASSISTED NANOPARTICLES

The aqueous leaf extract of Acacia Nilcotica was added to 0.025 M aqueous Zinc acetate and adjusted the pH 12 using sodium hydroxide (10%). This result in pale white in color. After stirring for half hour, the precipitate was washed against with distilled water followed by ethanol to get free of impurities. The

solution was in vacuumed dried with desiccators and zinc oxide nanoparticles which are characterized by SEM and TEM. During synthesis of these nanoparticles, Plant material contains various biological polymers which act as capping agent. These particles have 100-120 nanometres

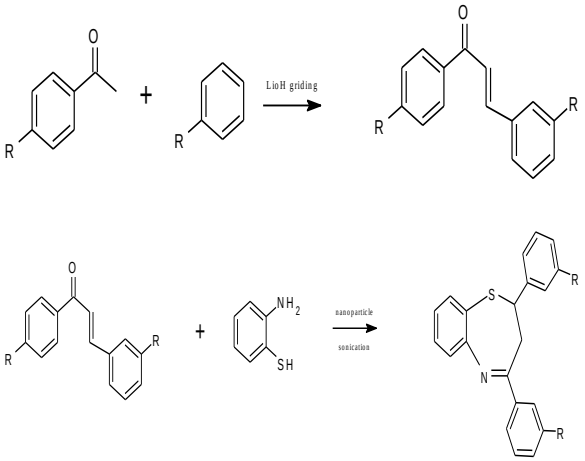
## IV. GENERAL PROCEDURE FOR THE SYNTHESIS OF BIS-[1,5]-BENZOTHIAZEPINES

To a mixture of bis-chalcone (10 mmol) and 2-aminobenzenethiol (10 mmol) in methanol was added along with triethylamine (10mmole) .Add 0.5 gram of plant assisted zinc oxide nanoparticles were added .This reaction mixture was subjected to sonication. Progress of the reaction was monitored by thin layer chromatography .After completion of the reaction, the reaction mixture was kept overnight at room temperature. The reaction mixture was poured in ice-water and solid obtained was filtered, washed with water and purified by column chromatography over silica gel using petroleum Hexane ethyl acetate (80:20 v/v) to afford the pure compound.

## V. RESULTS AND DISCUSSION

Bis-[1, 5]-benzothiazepines **(1-9)** incorporating two 1,5-benzothiazepine nuclei in a single molecule were synthesized . Bis-chalcone intermediates were prepared using lithium hydroxide as base and grinding method. Two α, β-unsaturated carbonyl groups at ortho and para position of –OH group in bis-chalcones were converted into 1,5-benzothiazepine rings by cyclocondensation reaction of bis-chalcones **(1-9)** (10 mmol) with 2-aminobenzenethiol (10 mmol) using plant assisted zinc oxide nanoparticles as catalyst. Formation of desired compounds **(1-9)** were confirmed by IR, $^{1}$H NMR,$^{13}$C NMR, IR spectrum of compound displayed band around 300 $cm^{-1}$ for –OH stretching of phenolic ring, band at 1500 $cm^{-1}$ for C=N stretching and band at 820, 756 $cm^{-1}$ for C-S stretching clearly reflecting the formation the formation of desired product. Presence of two 1,5-benzothiazepine rings, one at ortho and second at para position of –OH group in phenol was clearly indicated by the $^{1}$H NMR spectra, for example, in $^{1}$H NMR spectrum of compounds 1,5-benzothiazepine ring at para position of –OH in phenol displayed two doublet of doublet peaks for methylene and methine protons at δ 3.12 and δ 5.32 whereas 1,5-benzothiazepine ring at ortho position of –OH in phenol displayed two doublet of doublet peaks for methylene and methine protons at δ 3.57 and δ 5.48.

SCHEME 1:




Observation Table

| Sr.No | Substituent | Time min | Physical Constant 0c | % Yield |
|---|---|---|---|---|
| 1 | P-Chloro Benzaldehyde | 10 | 140 | 85 |
| 2 | P-Fluro Benzaldehyde | 10 | 141 | 90 |
| 3 | P-Methoxy Benzaldehyde | 15 | 138 | 70 |
| 4 | P-Methyl Benzaldehyde | 15 | 152 | 86 |
| 5 | P-Bromo Benzaldehyde | 10 | 136 | 85 |
| 6 | O-Fluro Benzaldehyde | 10 | 144 | 90 |
| 7 | P-nitro Benzaldehyde | 10 | 130 | 80 |
| 8 | 2 thiophene aldehyde | 15 | 170 | 85 |
| 9 | 2 furanaldehyde | 15 | 164 | 87 |

Spectral Data

**2,4-bis(E)-2-(4-chlorophenyl)-2,3-dihydro benzo [b][1,4]thiazepin-4-yl)phenol (1):** Yellowish brown solid, mp- 140$^{o}$C; FTIR : **ν** = 3328 (Ar-OH), 1580 (C=N), 750 (C-S) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$, 300 MHz): δ 3.03 (dd, 2H,) 3.17 (dd, 2H) 4.83 (dd, 1H, CH), 5.00 (dd, 1H), 6.54-8.19 (m, 19H, Ar-H ), 15.02 (s, 1H, Ar-OH );

**2,4-bis(E)-2-(4-flurophenyl)- 2, 3 dihydrobenzo [b] [1,4]thiazepin-4-yl)phenol (2):** Yellow brown solid, mp: 141$^{o}$C; FTIR : ν = 3170 (Ar-OH), 1616, 1507 (C=N) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$, 300 MHz): δ 3.07 (dd,), 3.51 (dd, 2H), 5.00 (dd, 1H, CH, J= 5.1 Hz, 6.3 Hz), 5.15 (dd, 1H), 6.66-7.70 (m, 19 H, Ar-H) ppm

## VI. CONCLUSION

In summary, we have synthesized chalcone using lithium hydroxide as base and griding method. We have synthesized and fully characterized bis-[1, 5]-benzothiazepines by cyclocondensation of bis-chalcones with 2-aminobenzenethiol using plant

assisted zinc oxide nanoparticles in good yield. This reaction was carried using sonication method .Aldehydes contain electron withdrawing groups, shows faster reaction than aldehydes having electron donating groups.

## ACKNOWLEDGEMENTS

We are thankful to Karmaveer Bhaurao Patil college Vashi navimumbai for providing the financial assistance. We are also thankful to the SAIF Punjab University for providing spectral analysis

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