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Ferrous Sulphate Catalysed Synthesis of 1, 5-Benzothiazepines using Sonication Method

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ABSTRACT: One step synthesis of various aromatic substituted, 1-5-benzothiazepines carried by the reaction of different substituted chalcone with ortho-aminothiophenol in sonication at 40°C using ferrous sulphate as catalyst. This reaction method is mild reaction condition and has very short reaction time as compared to the other conventional methods. The structural assignment of the final product has been done by spectral techniques or other techniques.

Keywords: Different substituted chalcone; ortho-aminothiophenol; ferrous sulphate and sonication short reaction time.

INTRODUCTION: Heterocyclic chemistry is important branch of which very inseparable from mankind because human being are totally dependent on the various life saving medicines from heterocyclic rings. We have focus mainly on the synthesis of nitrogen containing various heterocyclic compounds like Benzothiazepines derivatives mainly due to their very broad spectrum of biological and pharmacological activities.[1-3] Benzothiazepines is a pharmacophore present in many drugs, such as clozapine, emedastine (antihistaminic), cloxazolam, bromazepam, clobazam, dibenzepin cholecystokinin A and B antagonists, opioid receptor ligands, platelet-activating factor antagonists and HIV reverse transcriptase inhibitors and many others.[2-5] Besides from their biological importance, benzodiazepine derivatives are commercially used as dyes for acrylic fibres or various fibres. Especially 1,5 Benzothiazepines are important synthons or synthetic equivalent that can be used in the preparation of other fused ring compounds such as oxazino or furano triazolo, oxadiazolo, derivatives benzodiazepines.[5-7]

Generally benzodiazepines are synthesised using the direct condensation of o phenyl thio amines with α,β-unsaturated carbonyl compounds like chalcones and β-haloketones or ketones or other carbonyl compounds under various conditions. There are many methods available for the synthesis of 1,5 Benzothiazepines derivatives like Biginelli condensation,[7-8] through condensation of acetophenone derivatives, aldehydes and urea/thiourea or other carbonyl compounds using various Bronsted and Lewis acid catalysts are used.

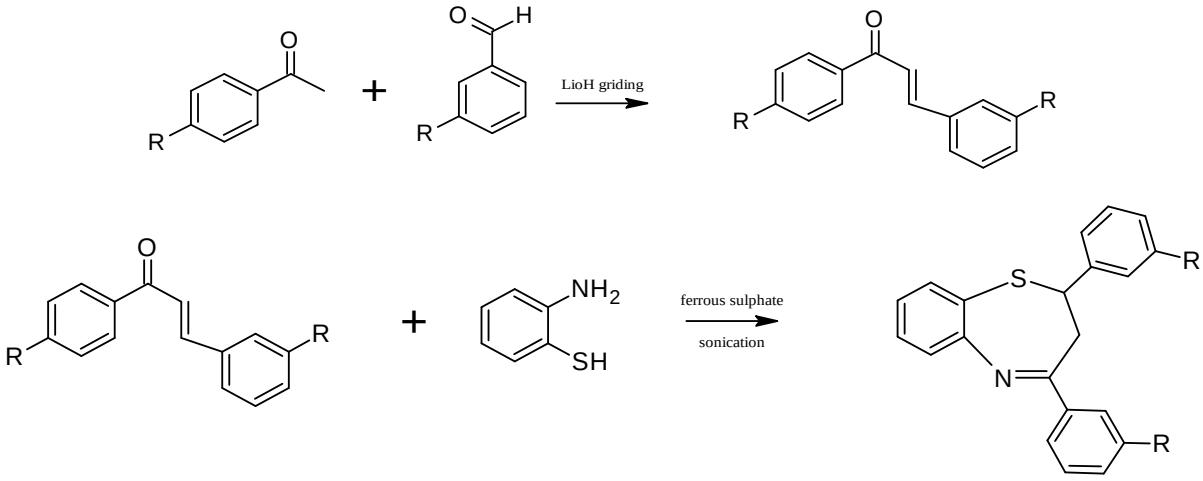
Considering, the potential of developing new routes to the synthesis of various heterocyclic compounds, the present investigation was aimed towards the synthesis of 2,4–diphenyl- 1,5–benzodiazepine derivatives using condensation reaction of 1,3-diaryl-2-propen-1-one derivatives and o-aminothiophenol using anhydrous ferrous sulphate as catalyst. Chalcones either natural or synthetic are well known to show biological activities such as antibacterial, antitumor, anti-inflammatory analgesic antipyretic, antimalarial , and anti tuberculosis and other biological activities . Chalcones are important starting materials for the synthesis of heterocyclic compounds such as thiazines, pyrazolines isoxazolines and Benzothiazepines etc. Most these heterocyclic compounds of these compounds are highly bioactive and are widely used in pharmaceuticcals and other. Due this wide range of pharmacological, industrial and synthetic applications as well pharmaceutical importance, the synthesis of 1, 5- benzodiazepines are the have been received considerable attention.

Generally, the method for the synthesis of 1,5-Benzothiazepines involves acid catalyzed α,β cyclocondensation o-phenylenediamine with unsaturated carbonyl compounds and its derivatives.[8-10] Ketones[11-12] using Piperidine-AcOH[13] $Ga(OTf)_3$[14]

HPW/SiO_2[15] MoO_3SiO_2[16] sulphated zirconia[17] and use of microwave irradiation technique[18] have well established methods of the synthesis. However, most of these methods suffer from several disadvantages such as long reaction time, expensive reagent, harsh reaction conditions and high reflux temperature, low yield, formation of impurities herein, we wish to report our results on the synthesis and some novel 1,5-benzodiazepine derivatives, using anhydrous ferrous sulphate as catalyst.

MATERIAL AND METHODS: Melting points of the compounds were determined in open capillary tubes and using paraffin's and are uncorrected, IR Spectra were recorded on Shimadzu FT-IR Spectrometer, 1H NMR was determined on a Bruker Advance II 400 Spectrometer against TMS used as internal standard. The compounds obtained are purified and purity is checked by thin layer chromatography (TLC).

General procedure for the preparation of benzodiazepines derivatives: A reaction mixture of unsaturated carbonyl compound (10 mmol) and ortho-aminothiophenol (10 mmol) in DMSO (10 ml) with few drops of morpholine along with ferrous sulphate was sonicated for 4-10 hrs. Reaction was monitored by using TLC. After completion of the reaction remove excess of solvent and pour reaction mixture in crushed ice. Filter the obtained product, and recrystallized from suitable solvent .Similarly all other derivatives were also synthesized. The product purified by recrystallization process in ethanol solvent.



[Reaction scheme]

Table 1: Observation table of 1, 5-Benzothiazepines using sonication method.

Sr. No	Substituent	Time hrs	Physical Constant 0c	% Yield
1	P-Chloro Benzaldehyde	4	142	90
2	P-Fluro Benzaldehyde	4	143	91
3	P-Methoxy Benzaldehyde	4.3	135	90
4	P-Methyl Benzaldehyde	4.5	154	96
5	P-Bromo Benzaldehyde	4	138	80
6	O-Fluro Benzaldehyde	4	148	85
7	P-nitro Benzaldehyde	4	133	94
8	2 thiophene aldehyde	4	172	60
9	2 furanaldehyde	4	166	65

RESULTS AND DISCUSSION: In the present work, we have reported the synthesis of 1,5-Benzothiazepines from the o-amino thiophene and chalcones respectively. A condensation reaction of chalcones (10 mmol) and o-phenylenediamine (10 mmol), was dissolved in DMSO with few drops of morpholine was sonicated for an appropriate time of 4-10 h. After completion of reaction, reaction mixture was worked-up to obtained product in good yield. This method for of 1, 5-Benzothiazepines using sonication method is best, eco-friendly, low cost, easy to carry out, good yield.

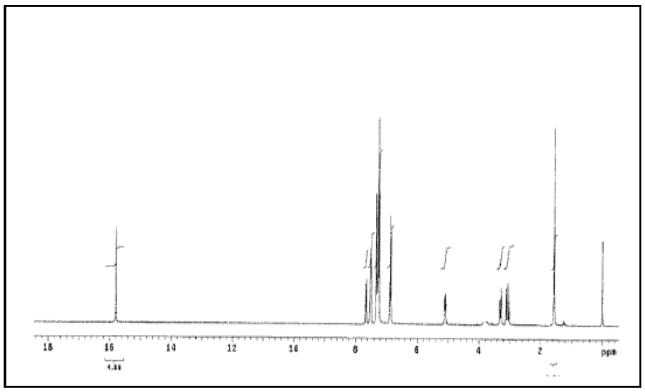


Figure 1: NMR Spectra of Benzothiazole Derivative.

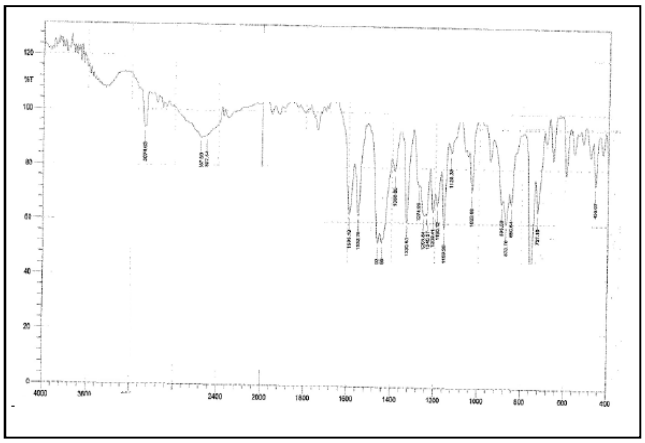


Figure 2: IR Spectra of Benzothiazole Derivative.

CONCLUSION: we have developed the ecofriendly approach for the synthesis of the Benzothiazepines, it gives better yield, high purity, and catalyst is recyclable.

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