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# Lanthanum Nitrate- Catalyzed Synthesis of New 2, 3-dihydro-1, 5-Benzothiazepines

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**ABSTRACT**

Simple and convenient procedure have been developed for the synthesis of optically active1,5-benzothiazepine derivatives by reaction of 2-aminothiophenolwith newly synthesized Chalcones under mild conditions in the presence of catalytic amount of Lanthanum Nitrate in short reaction time with excellent yield(75-80%)The products were tested for purity by TLC and characterized by M.P, IR and $^1$H NMR spectral studies.

**Key words:** Lanthanum Nitrate, 1, 5-Benzothiazepines, 2-Aminothiophenol, Chalcones, Mild Conditions.

## INTRODUCTION

For more than a century heterocyclic compounds have constituted one of the largest areas of research in organic synthesis[1]. Over the last two decades, synthesis of nitrogen and sulphur containing heterocyclic compounds especially 1, 5-benzothiazepines retained the interest of researchers due to the unique structural properties and broad spectrum of biological activities of these compounds[2]. Benzothiazepines and their derivatives play a vital role in the treatment of cardiovascular disorders[3], as $Ca^{2+}$ channel blockers[4], inhibitors of HIV-I integrase[5], antibiotics[6], muscle relaxants[7], and cytotoxic agents[8]. They are also known to have antimicrobial [9–11] and antihypertensive activities[12] besides being used in the treatment of diabetes[13], recently anticancer activity[14,15], hemodynamic effects[16] , antiulcer activity[17,18], and spasmolytic activities[19-23] have also been reported .Keeping in view this broad spectrum of biological activity associated with these compounds, for their synthesis several procedures are introduce in the literature [24,25], these include condensation of 2-aminothiophenol with carbonyl compounds, and different relationships have been observed between substrate and products formed [26-36], although these reaction have been investigated by different research groups, however to get newer insight in the formation of benzothiazepines, modification of

molecules and introduction of simple and convenient procedure for their synthesis are important and needed. The purpose of this study is to develop a simple convenient procedure for the synthesis of 2-thiophene, 4-aryl, 2, 3-Dihydro-1, 5-Benzothiazepines by condensation of 2-aminothiophenol with novel á-â unsaturated Ketones under mild conditions catalyzed by Lanthanum Nitrate [scheme-I].Earlier lanthanum Nitrate was used as a catalyst for the deprotection of acetonides[37], in selective deprotection of primary alcohols[38] , synthesis of 1,5-benzodiazepines from ketones[39] and for the synthesis of 1, 4-diazepines from the reaction of â-diketones/â-ketoester and ethylenediamine[40] .

## MATERIAL AND METHODS

Melting points were determined on an electronic melting point apparatus and are uncorrected. All $H^1$ NMR spectra were recorded on a Brucker AC 200 and Brucker MSL 300 spectrometers in DMSO and chemical shift were reported in ppm downfield from tetra methyl silane ($\delta$ =0.0ppm). Infrared spectra were recorded on a Perkin Elmer Infrared Spectrophotometer using KBr discs. TLC was performed on silica gel coated aluminum plates using ethyl acetate and pet ether (3:7 v/v) as eluent.

### Experimental Procedure (General)

A equimolar mixture of 2-aminothiophenol and Chalcones, Lanthanum Nitrate (10mole %]) in 10ml ethyl alcohol were stir on hotplate magnetic stirrer at room temperature for 30min, the corresponding 1,5-benzothiazepines were obtained in 75-85 % yield, Completion of the reaction was monitored by TLC. The results are summarized in table-I, the reaction mixture was Poured on crushed ice the solid crude product was washed with water and purified by recrystallisation using suitable solvent, which were further purified by column chromatography.

### Spectral data of selected compounds

**2-(Thiophene)-4-(4-Nitrophenyl) - 2, 3-dihydro-1, 5-benzothiazepine (3a)**

IR (KBr): (C=N) 1591$cm^{-1;}$ $^1$NMR (DMSO): $\delta$= 3.0(t, 1H, J=12.2Hz,), 3.4 (dd, 1H, J=12.2Hz, 4.4Hz), 5.0 (dd, 1H, J=12.2Hz, 4.4Hz), 6.1-7.0 (m, 11H).

**2-(Thiophene) - 4-(2-hydroxy, 3-chlorophenyl) - 2, 3-dihydro-1, 5-benzothiazepine (3c)**

IR (KBr): (C=N) 1600$cm^{-1;}$$^1$NMR (DMSO): $\delta$= 3.5(t, 1H, J=12.2Hz,), 3.2 (dd, 1H, J=12.2Hz, 4.4Hz), 5.0 (dd, 1H, J=12.2Hz, 4.4Hz), 6.72-7.2 (m, 10H).

**2-(Thiophene) - 4-(2-hydroxy, 3-chloro, 4-methylphenyl) - 2, 3-dihydro-1, 5-benzothiazepine (3d)**

IR (KBr): (C=N) 1599$cm^{-1;}$ $^1$NMR (DMSO): $\delta$= 2.0 (s, 3H), 3.0(t, 1H, J=12.2Hz,), 3.4 (dd, 1H, J=12.2Hz, 4.4Hz) 5.0 (dd, 1H, J=12.2HSz, 4.4Hz), 7.7-7.1 (m, 9H).

**2-(4-methylphenyl)-4-(2-hydroxyphenyl)-2, 3-dihydro-1, 5-benzothiazepine (3e)**

IR (KBr): (C=N) 1591$cm^{-1;}$ $^1$NMR (DMSO): $\delta$= 2.0 (s, 3H), 3.0(t, 1H, J=12.2Hz,), 3.4 (dd, 1H, J=12.2Hz, 4.4Hz), 5.0 (dd, 1H, J=12.2Hz, 4.4Hz), 7.7-7.1 (m, 12H).

**2-(4-chlorophenyl)-4-(2-hydroxyphenyl)-2, 3-dihydro-1, 5-benzothiazepine (3g)**

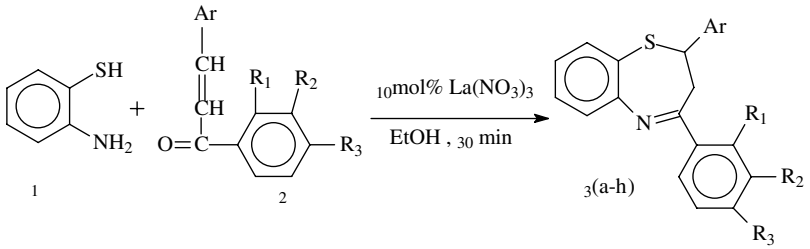
IR (KBr): (C=N) 1600$cm^{-1;}$ $^1$NMR (DMSO): $\delta$= 3.6 (t, 1H, J=12.4Hz)), 3.39 (dd, 1H, J=12.4Hz, 4.7Hz), 5.05 (dd, 1H, J=12.4Hz, 4.6Hz), 6.72-7.2 (m, 12H).

**2-(4-hydroxyphenyl) - 4-(2-hydroxyphenyl) - 2, 3-dihydro-1, 5-benzothiazepine (3h)**

IR (KBr): (C=N) 1599$cm^{-1;}$ $^1$NMR (DMSO): $\delta$= 3.03 (t, 1H, J=13.4Hz)), 3.39 (dd, 1H, J=12.4Hz, 4.7Hz), 5.0 (dd, 1H, J=12.6Hz, 4.8Hz), 6.72-7.2 (m, 12H).

## RESULTS AND DISCUSSION

One of the methods used so far for the syntheses of 1, 5-benzothiazepines is the reaction of unsaturated carbonyl compounds (Chalcones) with 2-aminothiophenols. We have studied such reactions by employing novel catalyst under mild reaction conditions. The results of synthesis of products 3(a-h) are summarized in table1.The starting compounds chalcones(2)is prepared by Claisen-Schmidt condensation of various substituted acetophenone and aromatic aldehydes in the presence of alcoholic KOH. The newly synthesize Chalcones with 2-aminothiophenol, and Lanthanum




**Scheme 1:**

Nitrate (10mole%]) in 10ml ethyl alcohol were stir on hotplate magnetic stirrer at room temperature for 30min,the reaction smoothly affords the corresponding 1, 5-benzothiazepines in 75-85 % yield, Completion of the reaction was monitored by TLC. The structures of the products were characterized by IR and $H^1$ NMR spectroscopy and melting points.

**Table 1: Characterization data of compounds 3a-h**

| Entry | Ar | R1 | R2 | R3 | Yield{%} | M.P{°C} |
|---|---|---|---|---|---|---|
| 3a |  | H | H | NO2 | 75 | 147-149 |
| 3b |  | H | H | OH | 80 | 140-142 |
| 3c |  | OH | Cl | H | 82 | 151-152 |
| 3d |  | OH | Cl | Me | 85 | 157-159 |
| 3e | Ph-($^4CH_3$) | OH | H | H | 77 | 158-160 |
| 3f | Ph-($^4OCH_3$) | OH | H | H | 75 | 193-195 |
| 3g | Ph-($^4Cl$) | OH | H | H | 75 | 172-174 |
| 3h | Ph-($^4OH$) | OH | H | H | 82 | 207-209 |

## CONCLUSIONS

In conclusion it can be summarized that, we have successfully synthesized 2, 3 dihydro 1, 5 benzothiazepine derivatives by applying a novel La $(NO_3)_3$ . $6H_2O$ catalyst which has the advantage of mild and efficient chemistry techniques, the work out is easy, reaction time is short, reaction conditions are mild and inexpensive catalyst with high yields of products, Selected original papers included in the references will help the reader to find the original information regarding 1, 5-benzothiazepine derivatives.

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