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## Synthetic and Pharmacological Profile of Thiopene: A Review

Nachiket S. Dighe<sup>\*1</sup>, Amol S. Balsane<sup>1</sup>, Ravindra B Laware<sup>2</sup>, Santosh S Dengale<sup>1</sup>, G S Asane<sup>2</sup> and Deepak S Musmade<sup>3</sup>

1. Department of Pharmaceutical Chemistry, Pravara Rural College of Pharmacy, Loni, MS, India-413736.
2. Department of Pharmaceutics, Pravara Rural College of Pharmacy, Loni, MS, India-413736.
3. Department of Pharmaceutical Chemistry, SRES's Sanjivani College of Pharmaceutical Education and Research, Kopergaon, Maharashtra, India-423603.

### ABSTRACT

Thiophene a five member heterocycles had been found with enormous biological activities with the suitable modifications in the structure. The present review is an attempt made to direct the attention of the researchers towards the thiopene ring for the development of newer chemical entities which are quite useful in the treatment of various life threatening diseases and disorders. This review article covers the most active thiopene derivatives that have shown considerable biological actions such as antimicrobial, anti-inflammatory. This review also discusses the structure-activity relationship of the most potent compounds. It can act as an important tool for medicinal chemists to develop newer compounds possessing thiopene moiety that could be better agents in terms of efficacy and safety.

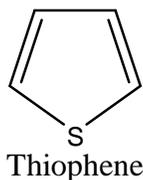
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\*Corresponding Author Email: nachiket1111@rediffmail.com

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## INTRODUCTION

Thiophene is a cyclic compound containing one Sulfur atoms in a five member ring. Thiazole are known from about eighty years and investigations in this field have intensified due to its applications in most diverse areas like dry synthesis, polymer as they give new aliphatic nitrogen compounds to other ring systems. Thiophene, containing a sulfur atom at 1 position, positions 2 and 5 are equivalent in the parent ring, as are the 3 and 4 positions. It is a heterocyclic, aromatic compound with formula  $C_4H_4S$ , chemical name is thiacyclopentadiene. Thiophene is taken from the Greek word *theion* means sulfur and *phaino* means shining. Consisting of a flat five membered ring, it is aromatic as indicated by its extensive substitution reactions.



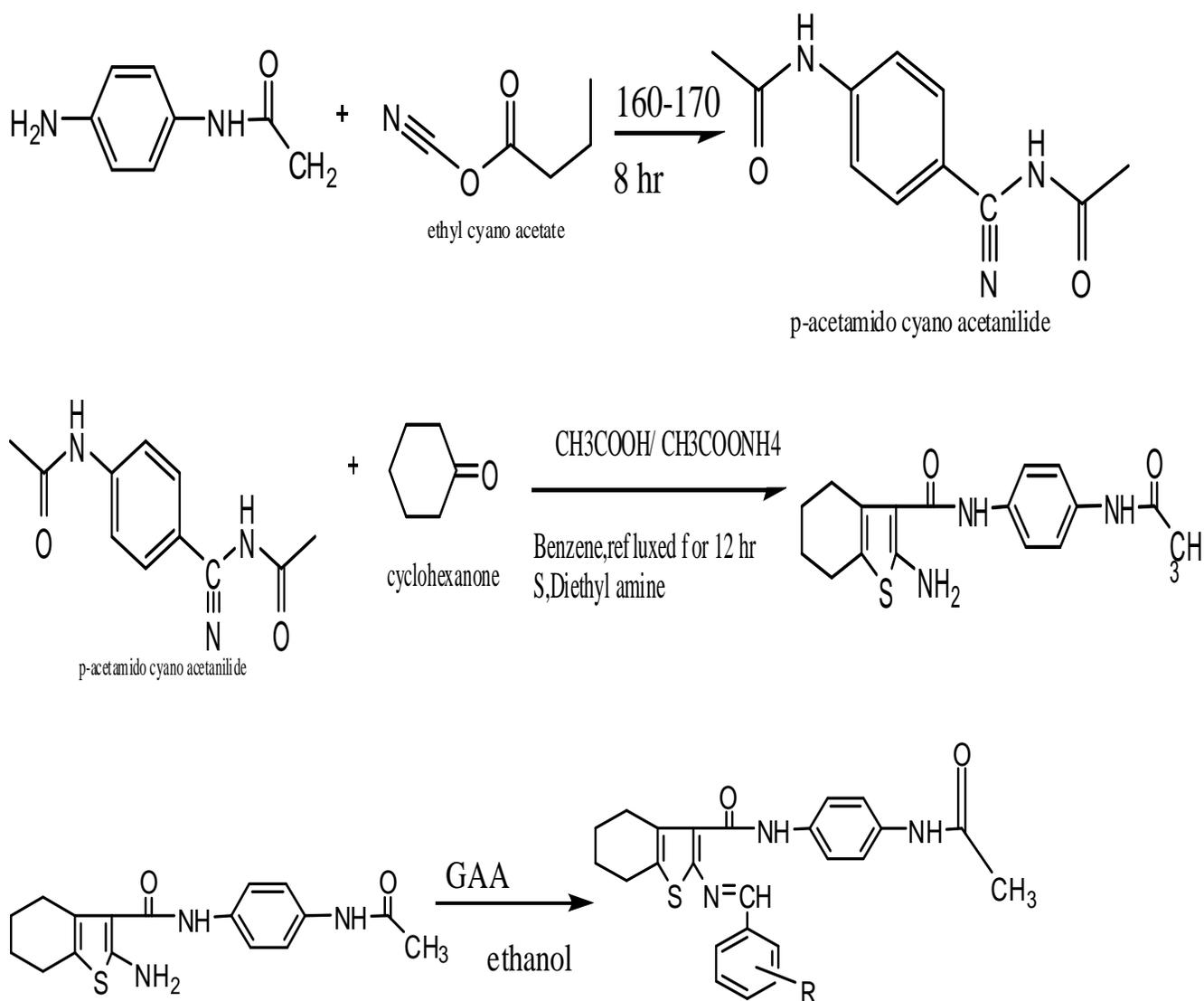
### Physical Properties of Thiophene:

Thiazole is a five membered heterocycle having four carbons, one Sulfer and two double bonds. Thiophene is an aromatic heterocyclic compound consisting of four carbon atoms and one sulfur atom in a five-membered ring. Compounds analogous to thiophene include furan and pyrrole where the S atom is replaced by O and NH, respectively. Thiophene is considered aromatic, although theoretical calculations suggest that the degree of aromaticity is less than that of benzene. The participation of the lone electron pairs on sulfur in the delocalized  $\pi$ -electron system is significant. Thiophenes are used as synthetic intermediates, taking advantage of the susceptibility of the carbon atoms 5 adjacent to sulphur to ward electrophilic reactions. It is considered to be aromatic and “ $\pi$ - excessive”. This is because the five  $sp^2$  – hybridized atoms may sustain a  $6\pi$ -electron system. Each carbon atom contributes one p-hybridized electron to the system and the lone pair provides the remaining two electrons 4. Thiophene is the sulphur analogue of furan, and its structure is very similar. Thiophene however has a higher degree of stabilization energy than furan, and is more aromatic in character as is borne out by its chemical reactions. There are several possible reasons for this: - one is that sulphur has a larger bonding radius than oxygen which allows the C-CC bond angles to widen a little, thus allowing some gain in stability by losing a little angle- compression strain, a second reason is that trivalent sulfur tolerates a positive charge better than oxygen. The sulfur atom carries an electron pair in  $sp^2$  hybrid orbital in the plane of the ring. The simple thiophenes are stable liquids which closely resemble the corresponding benzene derivatives in boiling point and even in smell. They occur in

coal tar distillates, and the discovery of thiophene in coal tar benzene provides one of the classic anecdotes of organic chemistry. Thiophene is from the Greek word, "theion" for sulfur and another Greek word "phaino" which means shining. Five membered heterocycles such as thiophene and pyrrole have widely been used as building blocks for the design of well-defined linear  $\pi$  conjugated oligomers and polymers.

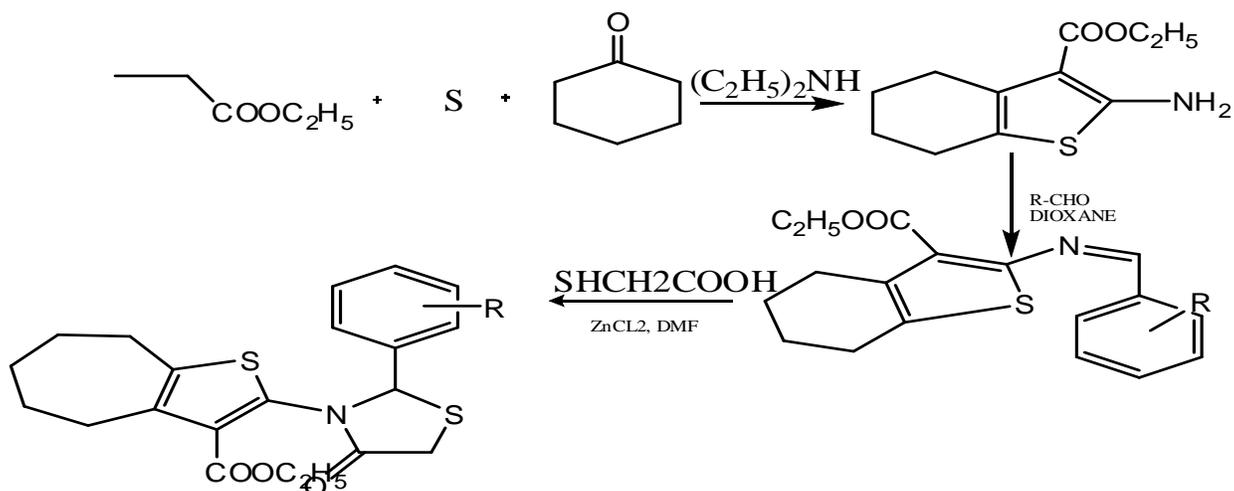
### Method of synthesis

1. Monica arora *et al* in the year 2012 had been reported with the synthesis, characterization and antimicrobial activity of some schiff bases Of 2-amino-n-(p-acetamidophenyl carboxamido)-4,5,6,7-tetramethylene Thiophenes.<sup>1,2</sup>

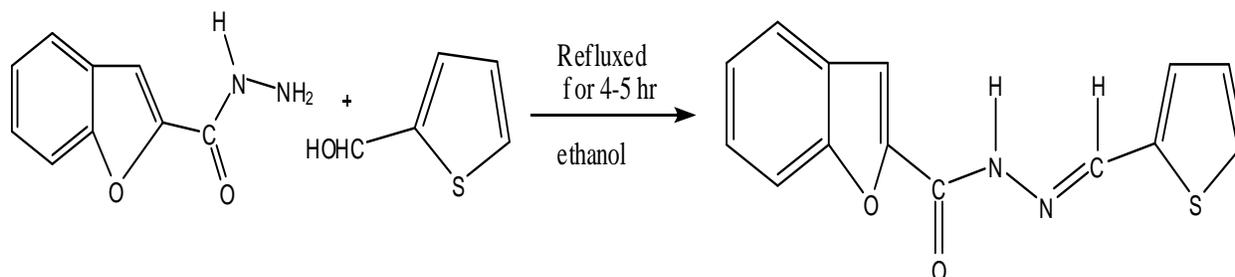


N-(4-acetanilido)-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide

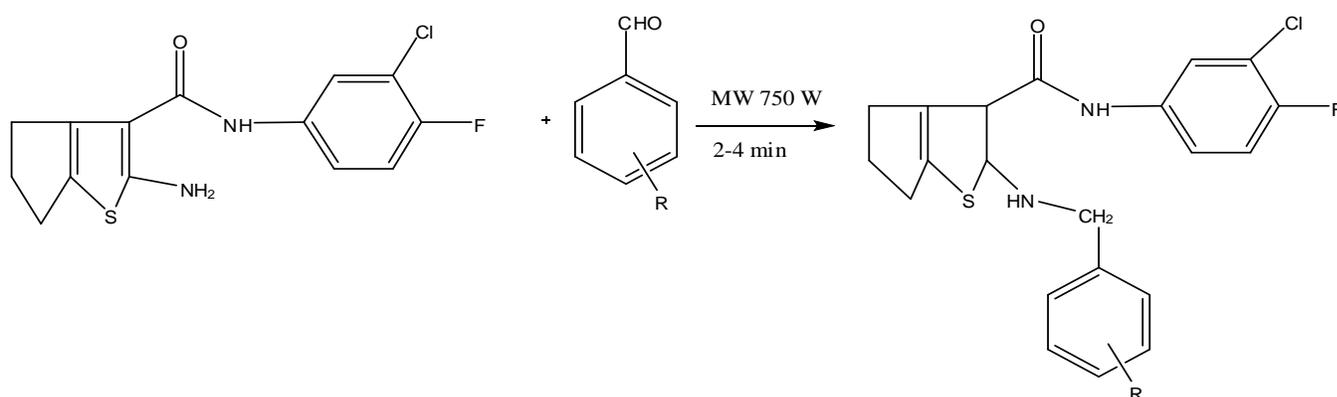
Raghav Mishra *et al* in the year 2012 had been reported with the Synthesis and antimicrobial evaluation of novel thiophene derivatives.<sup>3,4</sup>



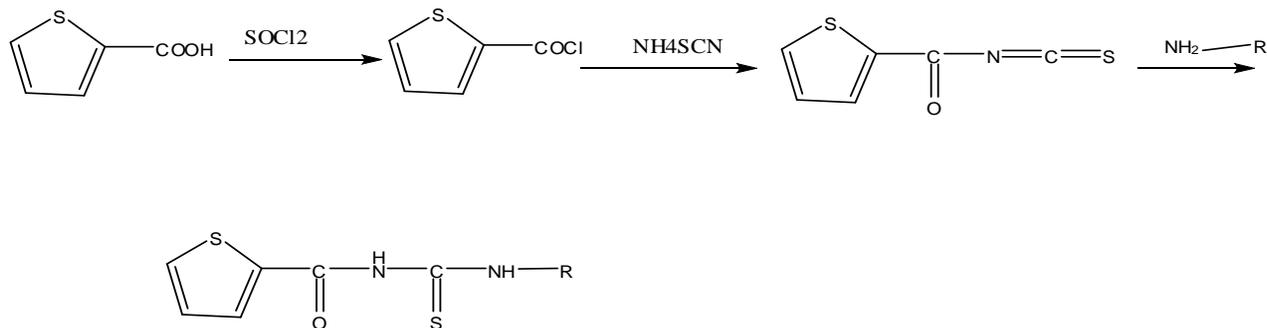
3. Madappa b. Halli *et al* in the year 2010 had been reported with the Synthesis, characterization, and biological activity studies of (E)-N\_ -((thiophen-2-yl)methylene)benzofuran- 2-carbohydrazide and its metal(II) complexes.<sup>5,6</sup>



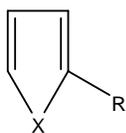
4. Satyendra deka *et al* in the year 2010 had been reported with the syntheses, characterization and *in-vitro* anti-inflammatory Activity of some novel thiophenes.<sup>7,8</sup>



5. Carmellina daniela bădiceanu *et al* in the year 2010 had been reported the synthesis and characterization of some biological active Compounds on the basis of 2-thiophene carboxylic acid With heterocyclic amines.<sup>9,10</sup>

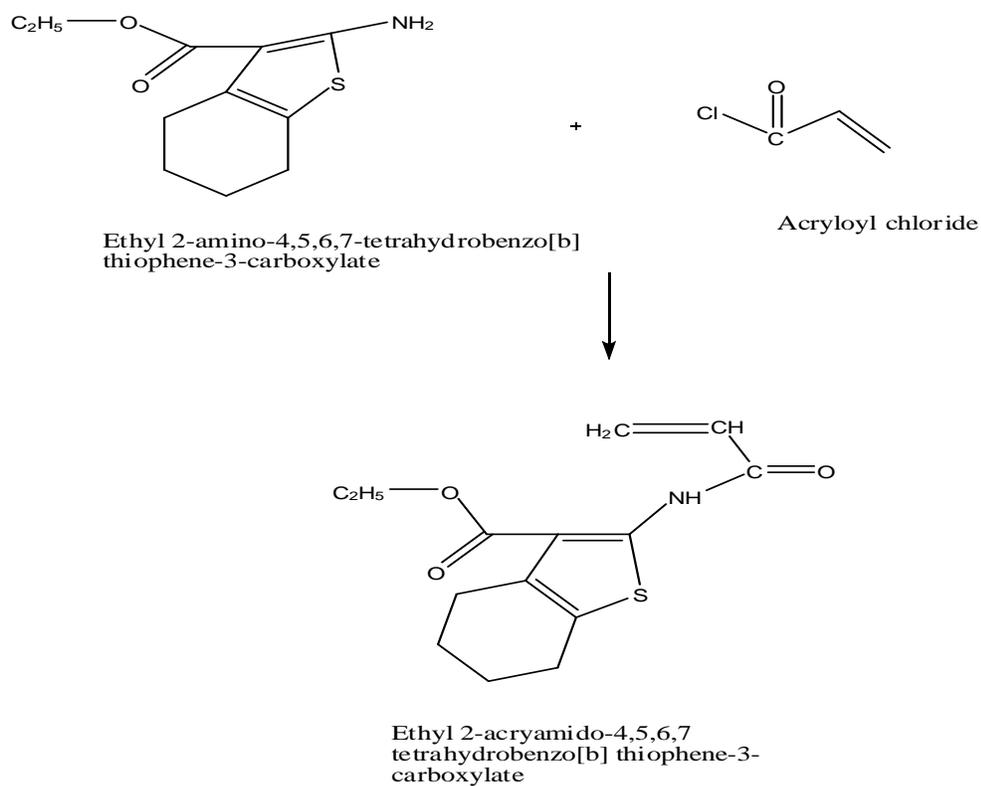


6. Flavia c. Meotti *et al* in the year 2003 had been reported thiophenes and furans derivatives: a new class of potential Pharmacological agents.<sup>11,12</sup>

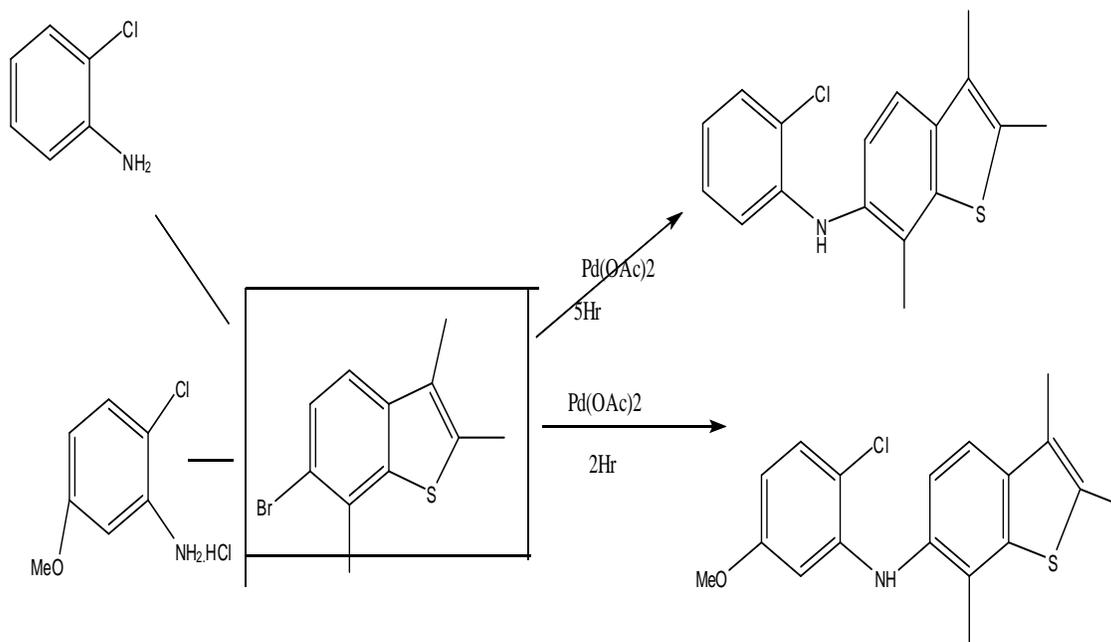


1-X=S; R= CH<sub>2</sub>OH  
 2-X=S; R=(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>OH  
 3-X=S; R=(CH<sub>3</sub>)C(OH)(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>

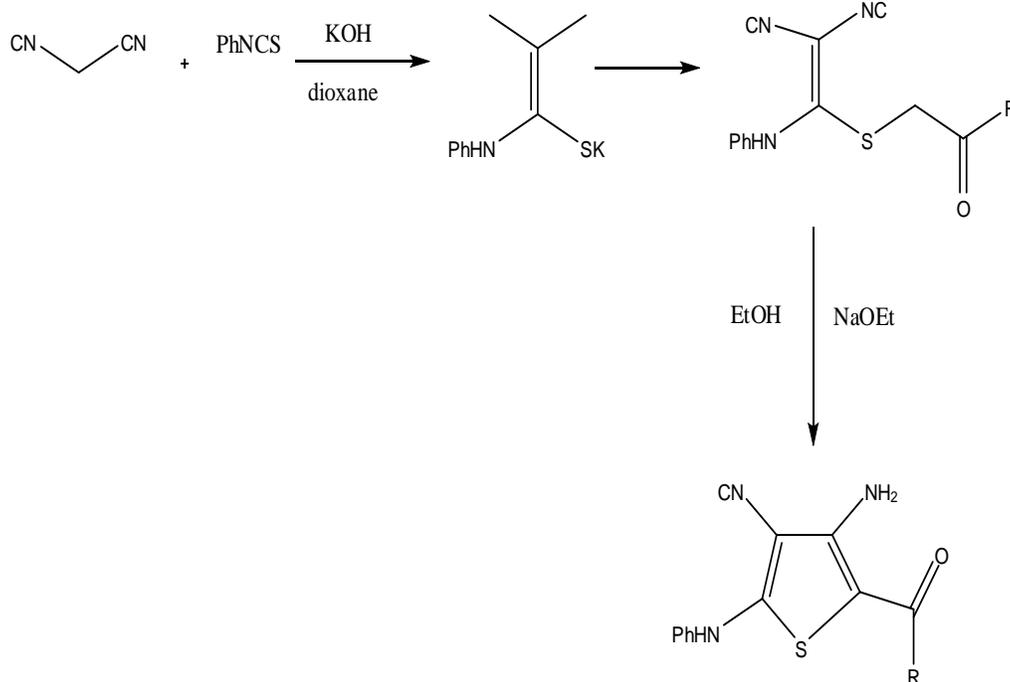
7. Maher Z. Elsabee, *et al* in the year 2011 had been reported Synthesis, characterization polymerization and antibacterial properties Of novel thiophene substituted acrylamide.<sup>13,14</sup>



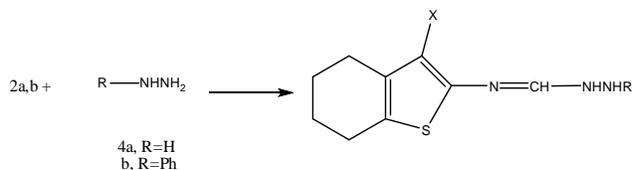
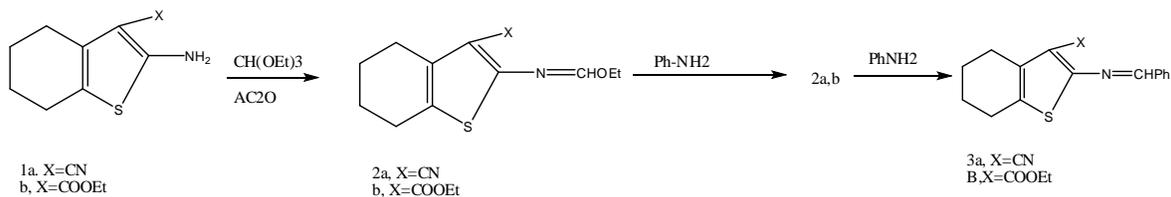
8. Maria-joão r. P. Queiroz *et al* in the year 2006 had been reported synthesis and antimicrobial activity studies of orthochlorodiarylamines and heteroaromatic tetracyclic systems in the benzo[b]thiophene series.<sup>15,16</sup>



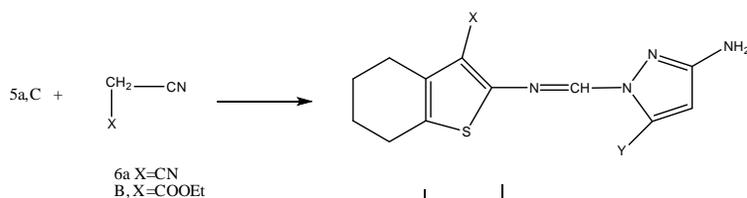
9. Ahmed M. M *et al* in the year 2007 had been reported Synthesis and Biological Evaluation of Some New Thienopyridine and Thienopyrimidine Derivatives.<sup>17,18</sup>



10. Rafat m. Mohareb *et al* had been reported cytotoxicity of novel 4,5,6,7-tetrahydrobenzo[B]thiophene derivatives and their uses as Anti-leishmanial agents.<sup>19,20</sup>

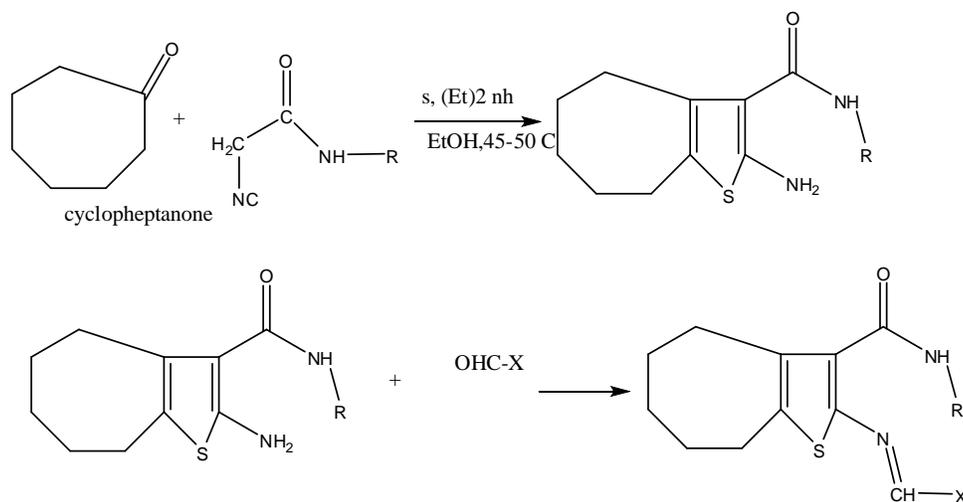


5	X	R
a	CN	H
b	CN	Ph
c	COOEt	H
d	COOEt	Ph

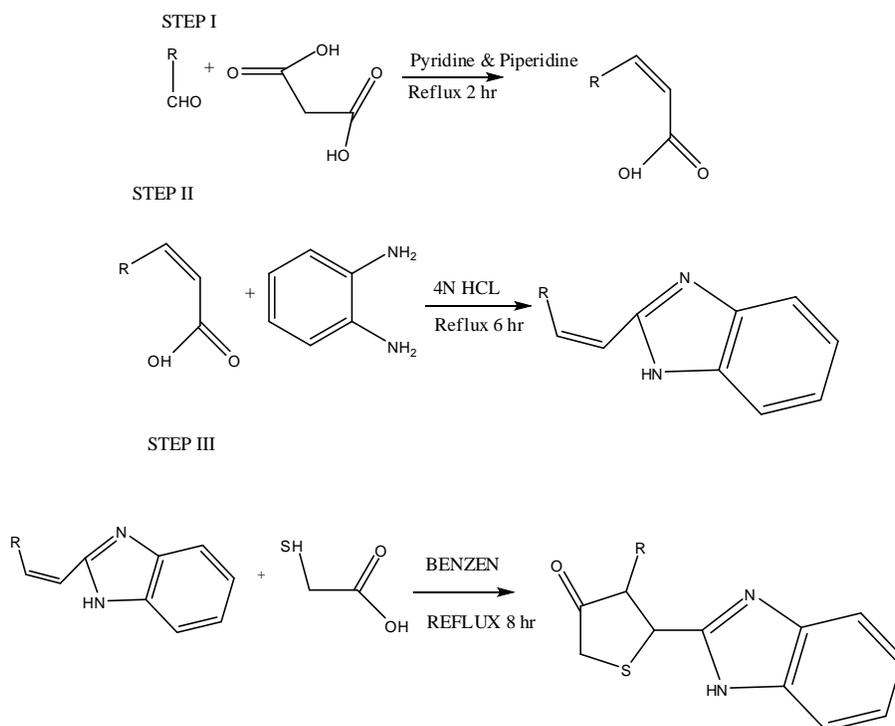


7	X	Y
a	CN	NH2
b	CN	OH
c	COOEt	NH2
d	COOEt	OH

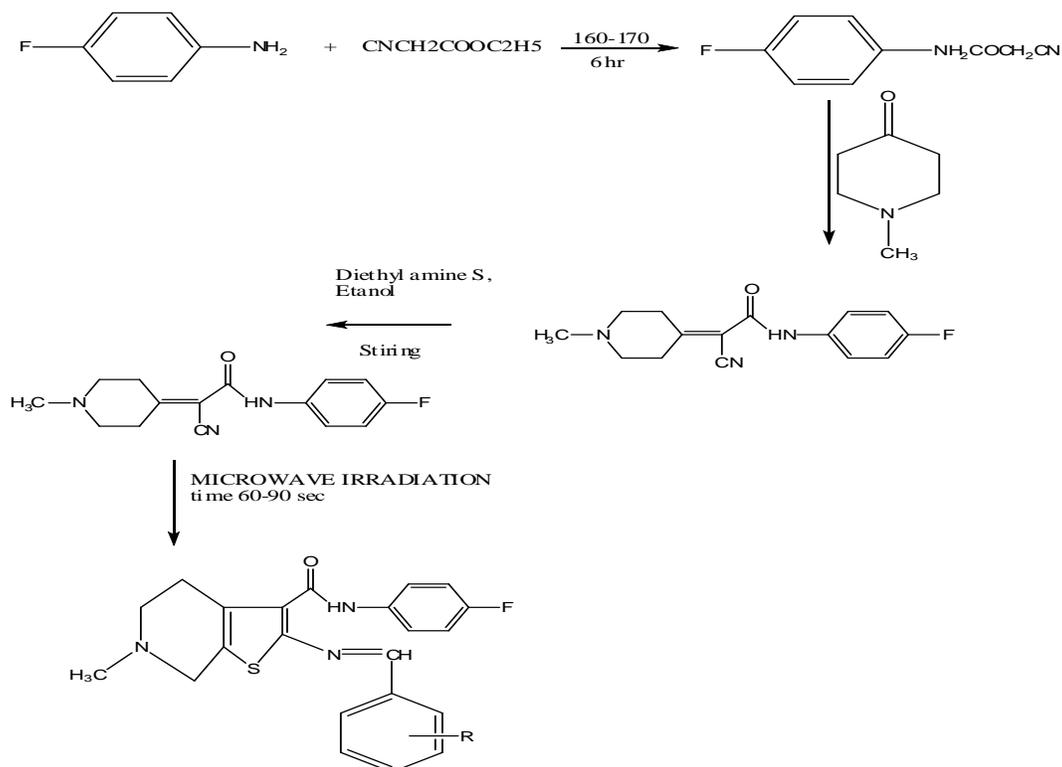
11. S.Mohan *et al* in the year 2003 had been reported The synthesis, Characterization and Antibacterial activity of Some Schiff Bas of 2-Amino-3-(N-Tolyl Carboxamide )-4,5-Pentamethylene Thiophenes.<sup>21</sup>



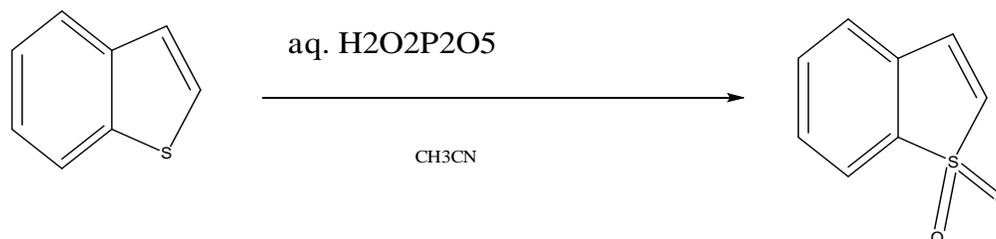
12. A. Jerad Suresh *et al* in the year 2011 had been reported The Design, synthesis, characterization and screening of thiophene derivatives for anti-inflammatory activity.<sup>22,23</sup>



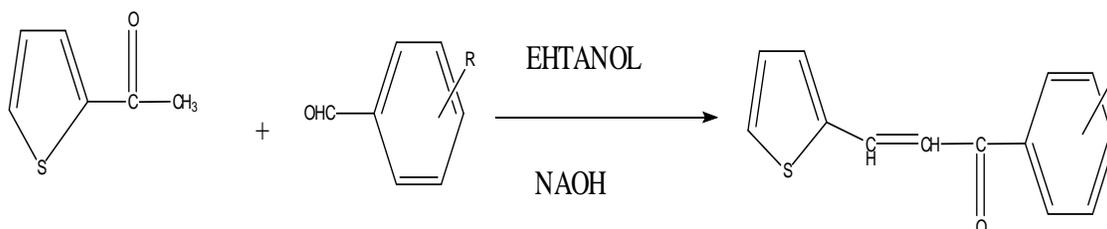
13. Prabodh Chander Sharma *et al* in the year 2011 had been reported Microwave Assisted Synthesis of Some 2-Amino-3-(p-Fluorocarboxanilido)-6- Methyl piperidino[4,3-b] Thiophenes and Their Antibacterial Evaluation.<sup>24</sup>



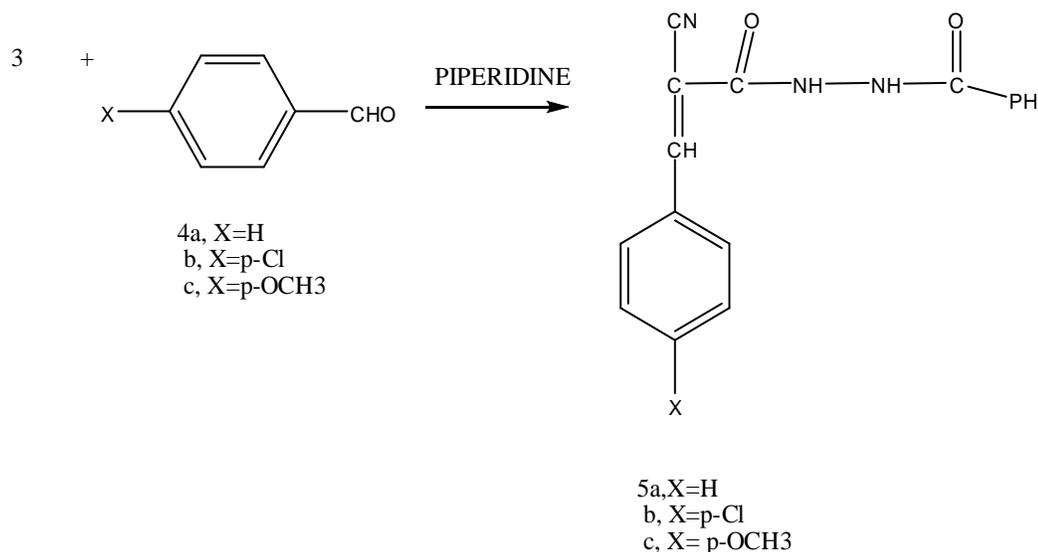
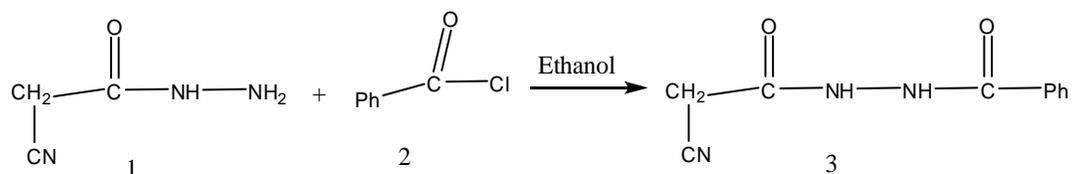
14. Dyeison Antonowet *et al* in the year 2009 had been reported Facile oxidation of electron-poor benzo [b] thiophenes to the corresponding Sulfoxes with an aqueous solution of H<sub>2</sub>O<sub>2</sub> and P<sub>2</sub>O<sub>5</sub>.<sup>25,26</sup>



15. Kamala Chand Gauta *et al* in the year 2013 Had Been Reported The Synthesis And Antimicrobial Activity Of Some Isoxazole Derivatives Of Thiophene.<sup>27,28</sup>



16. Rafat M. Mohareb *et al* in the year 2007 Had Been Reported Synthesis of Thiophenes, Azoles and Azines with Potential Biological Activity by Employing the Versatile Heterocyclic Precursor N-Benzoycyanoacetylhydrazine.<sup>28</sup>



## CONCLUSION

The plethora of research subscribed in this review indicates a wide spectrum of pharmacological activities exhibited by thiopene. The biological profiles of these new generations of thiopene would represent a fruitful matrix for further development of better medicinal agents.

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