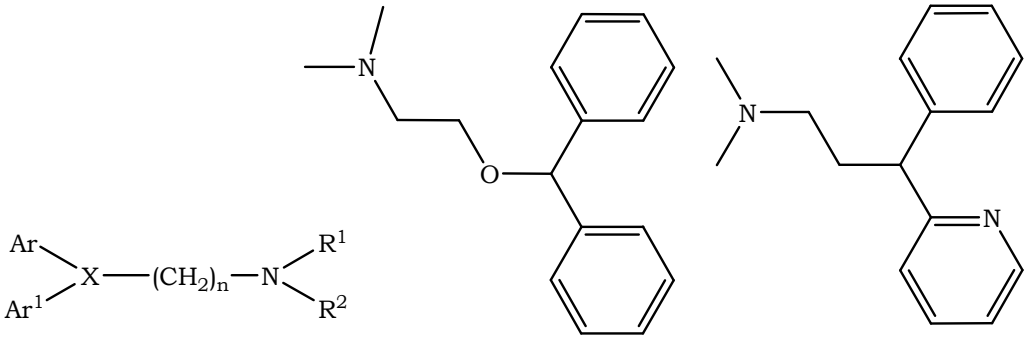
3. AIMS AND OBJECTIVES

The first generation antihistamines like Diphenhydramine and Pheniramine are effective in the allergic symptoms at cheaper cost, but they cause sedation and dry mouth due to their ability to cross blood-brain barrier and lack of specificity to the H_1-receptor.[322] First generation compounds possess a common feature of two aryl or heteroaryl rings linked through the side chain to an aliphatic tertiary amine.[323]



H_1-antihistamines Pharmacophore **Diphenhydramine** **Pheniramine**

Figure 3: First generation antihistamines

The second generation H_1-antihistamines like terfenadine, cetirizine and astemizole[324] have a greatly improved benefits compared to their predecessors. These drugs have limited potential to cross the blood-brain barrier and possess the higher H_1 receptor specificity[324] and are labeled as “non sedative antihistamines”. Many of the structural features of first generation compounds are present in these compounds also.

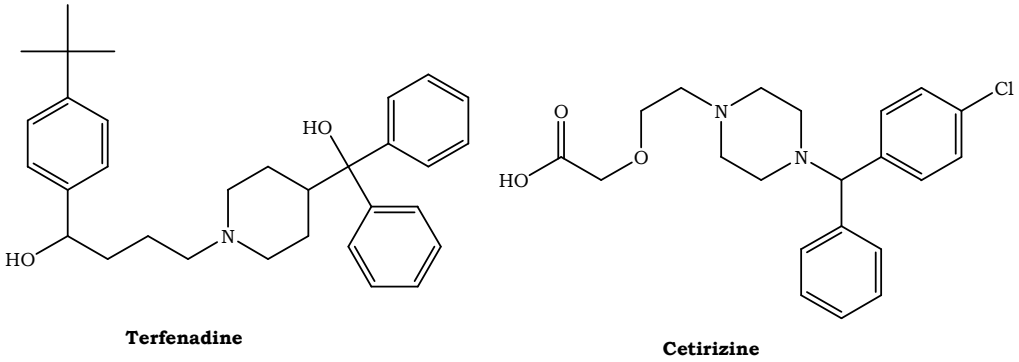


Figure 4: Second generation antihistamines

Quinazolines and substituted quinazolines exhibit excellent antihistaminic activity.[325-327] In our earlier studies, we have reported the quinazoline derivatives as potent antihistamines with least sedation.[328-330]

In continuation of our efforts in the development and identification of novel H_1-antihistamines **(Fig. 5)**, in the present study we have planned to synthesize some novel quinazolines by incorporating aryl/substituted aryl group at N-3 position and substitutedpropylthio group at C-2 position of quinazoline nucleus.

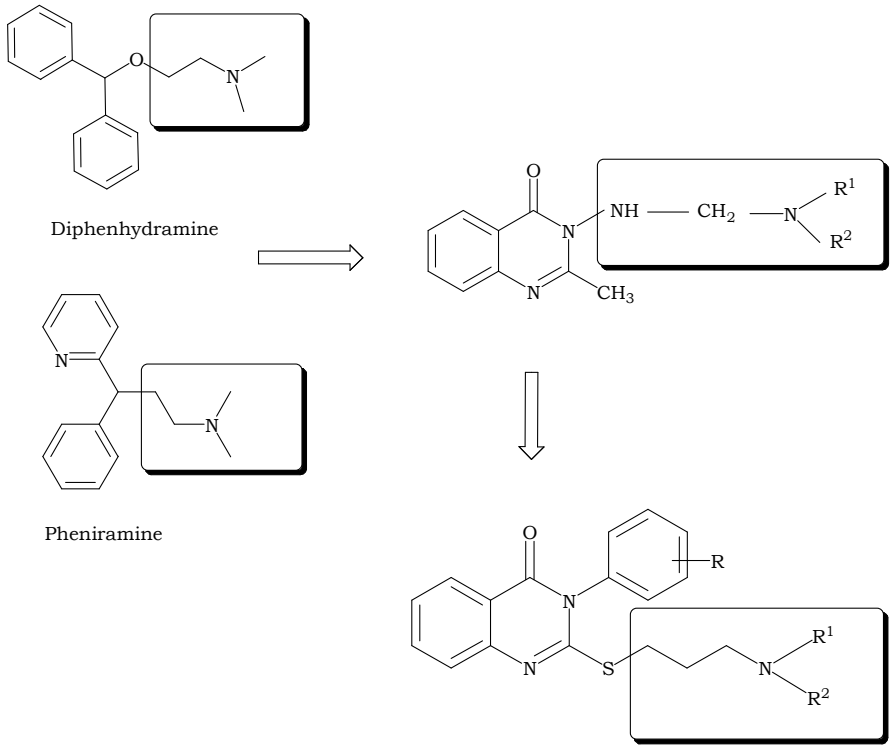
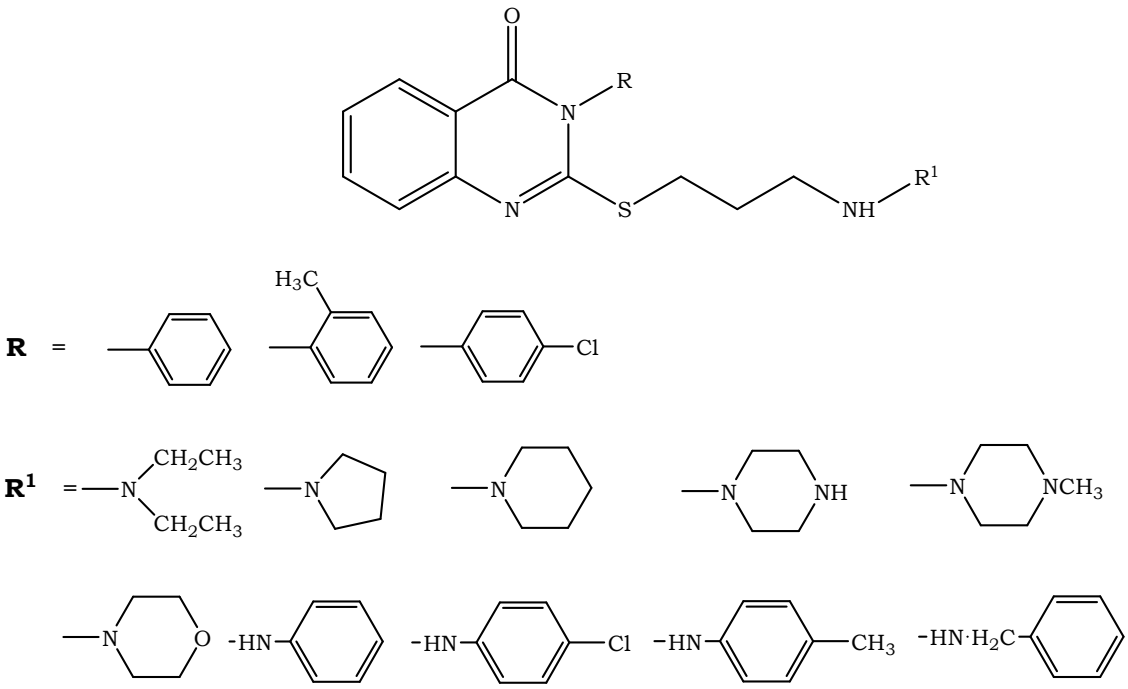


Figure 5: Lead generation of title compounds

It has been proposed that for H_1-antihistaminic activity, a compound should have the above mentioned pharmacophore (heterocyclic quinazoline ring linked via the side chain to an aliphatic tertiary amine). In view of these, a series of 3-(phenyl/substitutedphenyl)-2-(3-substitutedpropylthio) quinazolin-4(3*H*)-ones have been proposed to synthesize and study their H_1-antihistaminic activity potential by performing *in vivo* H_1-antihistaminic activity study on conscious guinea pigs. As sedation is one of the major draw backs associated with H_1-antihistamines, the test compounds will also be studied for their sedative potential.

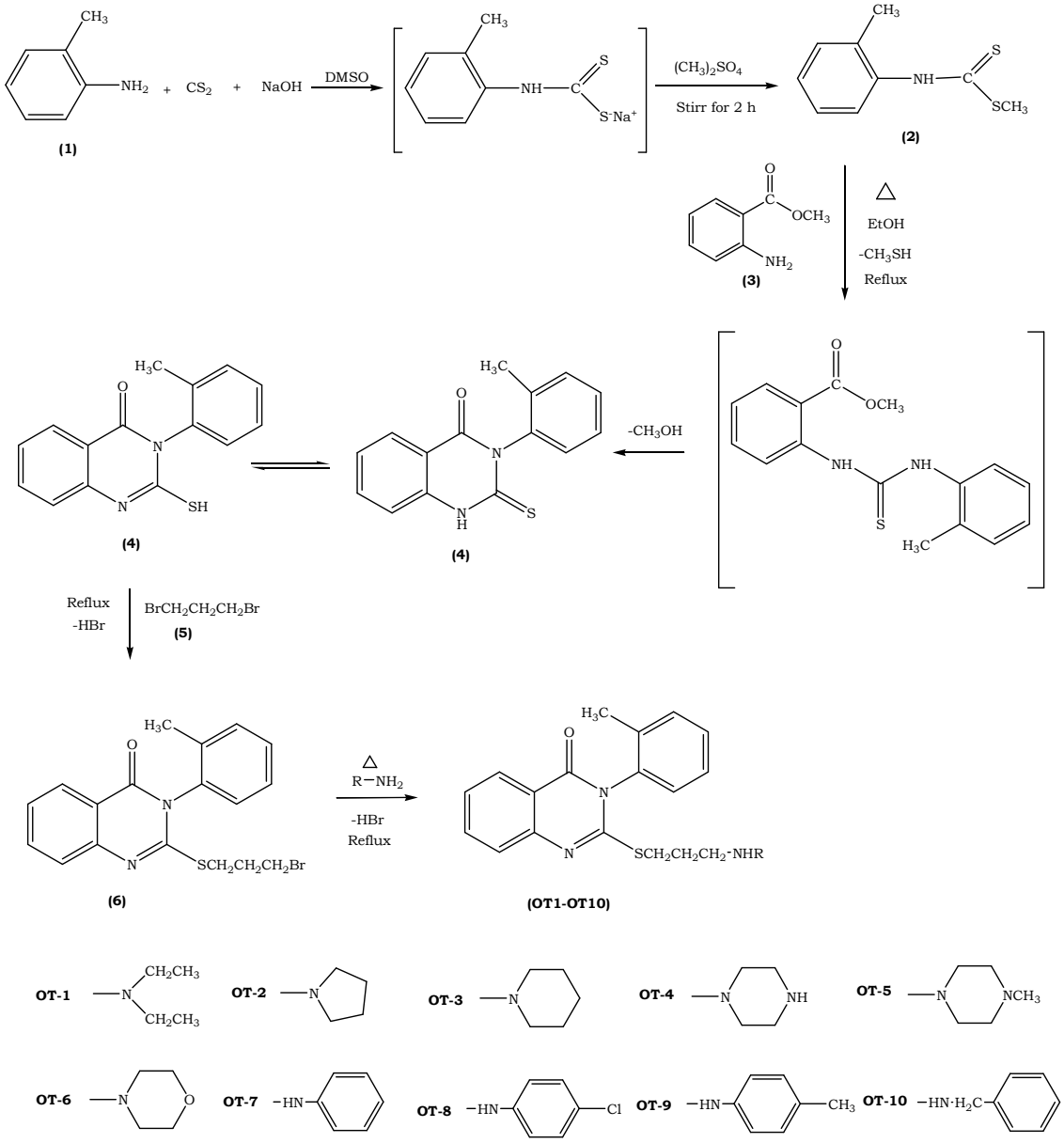


Thus the aims and objectives of the present work are summarized as follows:

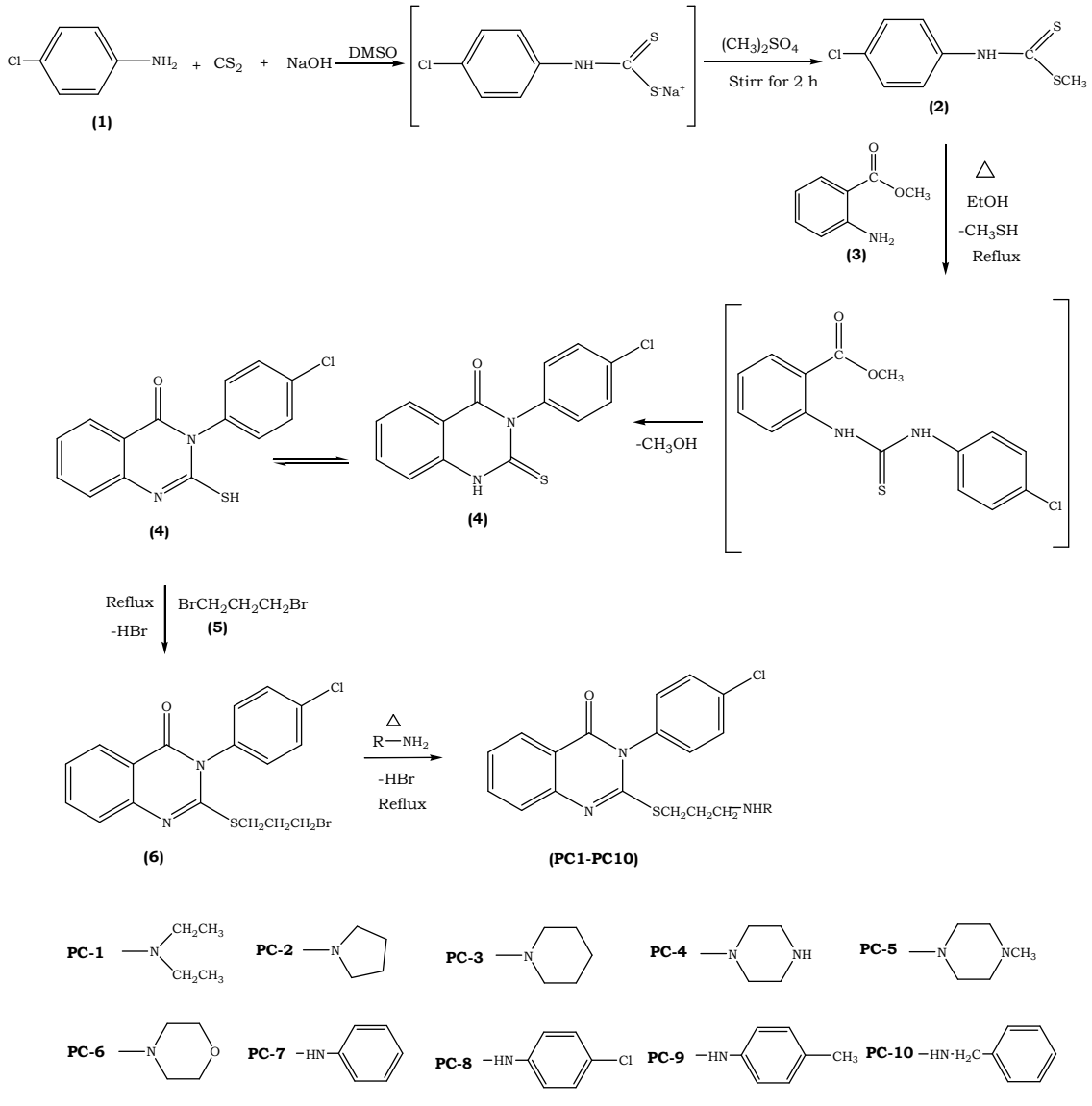
- To synthesize a variety of 2-(3-substituted propylthio)-3-(phenyl/substituted phenyl) quinazolin-4(3*H*)-ones.
- To characterize the synthesized compounds by IR, NMR and Mass spectra.
- To evaluate the synthesized compounds for their antihistaminic activity.
- To determine the sedative potential of the test compounds.
- To identify the active compounds for further exploitation.

The title compounds are planned to synthesize by the following synthetic route depicted in the scheme 1, scheme 2 and scheme 3.

Scheme 1: Synthesis of 3-(2-methyl phenyl)-2-(3-substitutedpropylthio) quinazolin-4(3*H*)-ones (OT1 – OT10)



Scheme 2: Synthesis of 3-(4-choloro phenyl)-2-(3-substituted propylthio) quinazolin-4(3*H*)-ones (PC1 – PC10)



Scheme 3: Synthesis of 3-(phenyl)-2-(3-substitutedpropylthio) quinazolin-4(3*H*)-ones (Ph1 – Ph10)