PREFACE

This thesis entitled “Synthesis, characterization and biological activities of some N, S-containing simple and condensed heterocycles” has been discussed in the following eight chapters.

Chapter 1: This is an introductory chapter, which deals with a brief account of synthesis, reactions and biological activities of some N, S-containing simple and condensed heterocycles based on the publications appearing in the chemical literature up to 2006.

Chapter 2: This chapter deals with the synthesis, characterization and biological activities of some new thiazolopyrimidine derivatives. Synthesis of some new ethyl-7-methyl-5-(4-methylthiophenyl)-2-(substituted arylidene/5-aryl-2-furfurylidene)-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]-pyrimidin-6-carboxylates by the one pot condensation of ethyl-6-methyl-4-(4-methylthiophenyl)-2-thioxo-1,2,3,4-tetrahydro-pyrimidin-5-carboxylate with mono-chloroacetic acid and various substituted benzaldehydes/5-aryl-furan-2-carboxaldehydes in the presence of anhydrous sodium acetate in acetic acid-acetic anhydride medium is reported. Ethyl-6-methyl-4-(4-methylthiophenyl)-2-thioxo-1,2,3,4-tetrahydro-pyrimidin-5-carboxylate was synthesized following the Biginelli procedure. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, 1H-NMR and mass spectral studies. These compounds were further screened for their in vitro antibacterial, antitubercular and antifungal activities. The results of such studies are described in this chapter.

Chapter 3: This chapter deals with the synthesis, characterization and biological activities of some triazolothiadiazole and triazolothiadiazine derivatives. The condensation of 4-amino-3-(4-methylthiobenzyl)-5-mercapto-1,2,4-triazole with various substituted arylcarboxylic/aryloxyacetic acids in the presence of phosphorus oxychloride afforded a series of 6-(substituted aryl/aryloxymethyl)-3-(4-methylthiobenzyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles. The condensation of 4-amino-3-(4-methylthiobenzyl)-5-mercapto-1,2,4-triazole with various substituted phenacyl bromides in the presence of anhydrous sodium acetate afforded a series of
7H-6-(substituted aryl)-3-(4-methylthio benzyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazines. 4-Amino-3-(4-methylthiobenzyl)-5-mercapto-1,2,4-triazole was obtained from 4-(methylthiophenyl) acetic acid hydrazide by the treatment with carbon disulfide in the presence of potassium hydroxide followed by condensation of the intermediate potassium dithiocarbazinate with hydrazine hydrate. 4-(Methylthiophenyl) acetic acid hydrazide was obtained from 4-(methylthiophenyl) acetic acid on esterification followed by the treatment with hydrazine hydrate. 4-(Methylthiophenyl) acetic acid was obtained by the base catalyzed hydrolysis of the corresponding 4-(methylthiophenyl) acetonitrile. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, $^1$H-NMR and mass spectral studies. These compounds were further screened for their in vitro antibacterial, antitubercular and antifungal properties. The results of such studies are described in this chapter.

Chapter 4: This chapter deals with the synthesis, characterization and biological activities of some triazinothiadiazole and triazinothiadiazine derivatives. The condensation of 4-amino-6-(4-methylthiobenzyl)-3-mercapto-1,2,4-triazin-5(4H)-one with various substituted arylcarboxylic/aryloxyacetic acids in the presence of phosphorus oxychloride afforded a series of 7-(substituted aryl/aryloxymethyl)-3-(4-methylthiobenzyl)-1,3,4-thiadiazolo[2,3-c]-1,2,4-triazin-4-ones. The condensation of 4-amino-6-(4-methylthiobenzyl)-3-mercapto-1,2,4-triazin-5(4H)-one with various substituted phenacyl bromides in the presence of anhydrous sodium acetate followed by the cyclization of the intermediate triazinone derivatives in the presence of concentrated sulphuric acid afforded a series of 8H-7-(substituted aryl)-3-(4-methylthiobenzyl)-1,3,4-thiadiazino[2,3-c]-1,2,4-triazin-4-ones. 4-Amino-6-(4-methylthiobenzyl)-3-mercapto-1,2,4-triazin-5(4H)-one was obtained by the condensation of 4-(4-methylthiobenzylidene)-2-methyl-oxazol-5-one with thiocarbohydrazide. 4-(4-Methylthiobenzylidene)-2-methyl-oxazol-5-one was obtained by the condensation of acetyl glycine with 4-methylthiobenzaldehyde in the presence of anhydrous sodium acetate. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, $^1$H-NMR and mass spectral studies. These compounds were further screened for their in vitro antibacterial, antitubercular and antifungal properties. The results of such studies are described in this chapter.
Chapter 5: This chapter deals with the synthesis, characterization and biological activities of some Mannich bases. The condensation of 4-amino-3-(4-methylthiobenzyl)-5-mercapto-1,2,4-triazole with various substituted benzaldehydes in the presence of concentrated sulphuric acid afforded a series of 3-(4-methylthiobenzyl)-4-(substituted arylidene)amino-5-mercapto-1,2,4-triazoles (Schiff bases). These Schiff bases were aminomethylated using formaldehyde and morpholine/N-methylpiperazine to afford two series of Mannich bases, namely, 1-(morpholino)methyl-3-(4-methylthiobenzyl)-4-(substituted arylidene)amino-1,2,4-triazol-5-thiones and 1-(N-methylpiperazino)methyl-3-(4-methylthiobenzyl)-4-(substituted arylidene)amino-1,2,4-triazol-5-thiones. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, $^1$H-NMR and mass spectral studies. These compounds were further screened for their in vitro antibacterial, antitubercular and antifungal properties. The results of such studies are described in this chapter.

Chapter 6: This chapter deals with the synthesis, characterization and biological activities of some pyrazoline derivatives. The condensation of 4-methylthiobenzaldehyde with various substituted acetophenones in the presence of potassium hydroxide under Claisen-Schmidt reaction conditions afforded a series of 1-(substituted aryl)-3-(4-methylthiophenyl)-2-propen-1-ones (chalcones). These chalcones were treated with hydrazine hydrate/phenyl hydrazine in glacial acetic acid medium to afford two series of pyrazolines, namely, 1-acetyl-3-(substituted aryl)-5-(4-methylthiophenyl)-2-pyrazolines and 1-phenyl-3-(substituted aryl)-5-(4-methylthiophenyl)-2-pyrazolines. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, $^1$H-NMR and mass spectral studies. These compounds were further screened for their in vitro antibacterial, antitubercular and antifungal properties. The results of such studies are described in this chapter.

Chapter 7: This chapter deals with the nonlinear optical (NLO) studies and crystal structure studies of some 1-(substituted aryl)-3-(4-methylthiophenyl)-2-propen-1-ones (chalcones). The powder second harmonic generation (SHG) efficiency of the chalcones has been studied and their NLO efficiency was determined by comparison with urea as the standard. Some of the chalcones have shown good nonlinear optical
response and hence can act as effective organic second order nonlinear optical materials. The single crystal structure determination has been carried out for some of these chalcones and the crystal structure data of such compounds are presented in this chapter.

Chapter 8: Eighteen newly synthesized compounds reported in this thesis were evaluated for their anticancer activity by NIH, Bethesda, Maryland, U.S.A under the Developmental Therapeutic Program (DTP). These compounds were acquired by NIH for screening against a panel of 60 cell lines derived from nine cancer types namely, leukemia, lung, colon, CNS, melanoma, ovarian, renal, prostate and breast. It is interesting to note that twelve compounds have emerged as “ACTIVE” in the anticancer assay. The results of such studies are embodied in this Chapter.