Name of Candidat : Zeinab Mohamed Abd el wahab Hassan
Degree M.Sc
Title of Thesis"

Synthesis and reactions of some heterocyclic compounds Containing Nitrogen and Sulphure"

Supervisors:
1- Prof. Dr./ Abdel Moneim Abdel Salam Maklof

Prof. Dr. Ayman Mohamed Salah Youssef 3- Dr. Wael Abdel Gaid Arafa

Approval / /2014 Department Chemistry

ABSTRACT

This thesis describes synthesis of 6-amino-4-(4-chlorophenyl) -3,4-dihydro-2*H*-thiopyran-3,5- dicarbonitrile (Ia) , 6-amino-3,4-dihydro-4-(4-methoxyphenyl)-2*H*-thiopyran-3,5-di-carbonitrile(Ib) from reaction between 2-cyano-3-aryl prop-2-enethioamide and acrylonitrile or ethyl acrylate in refluxing acetic acid. The product confirmed by spectral data and elemental analysis. Thesis described also reaction of Compound (Ia,b) with different reagents namely: formic acid, formamide , carbon disulfide, and acetic anhydride afforded 4,5,6,7-tetrahydro-4-oxo-5-aryl-3*H*-thiopyrano-[2,3-d]-pyrimidine-6-carbonitriles, 4-Amino-6,7-dihydro-5-aryl-5*H*-thiopyrano[2,3-d]-pyrimidine-6-carbonitrile, 2,3,4,5,6,7-hexahydro-5-aryl-2,4-dithioxo-1*H*-thiopyrano -[2,3-d]-pyrimidine-6-carbonitrile (IIa,b), 4,5,6,7-tetrahydro-2-methyl-4-oxo-5-aryl-3*H*-thiopyrano -[2,3-d]-pyrimidine-6-carbonitrile respectively. Reaction between I a,b urea, thiourea , and ammonium thiocyanate in sodium ethoxide solution gave 4-amino-2,5,6,7-tetrahydro-2-oxo-5-aryl-1*H*-thiopyrano-[2,3-d] pyrimidine-6 –carbonitrile, 4-amino-2,5,6,7-tetrahydro-2-thioxo-5-aryl-1*H*-thiopyrano-[2,3-d]-pyrimidine-6-carbonitrile (IIIa,b). Fusion of (Ia,b) with benzyl amine gave 6-amino-1-benzyl-1,2,3,4-tetrahydro-4-arylpyridine-3,5-dicarbonitrile derivatives. Reaction of Ia,b with each of malonitrile and ethyl acetoacetate in ethanol afforded 5,7-diamino-3,4-dihydro-4-aryl-2*H*-thiopyrano[2,3-b]-pyridine-3,6-dicarbonitrile, 5-amino-3,4,7,8-tetrahydro-7-oxo-4-aryl-2*H*-thiopyrano[2,3-b]-pyridine-3,6-dicarbonitrile(Iva,b)derivatives. Reaction of compound IV with $POCl_3$ followed by reaction with hydrazine hydrate and cyclization with HCl gave 4-diamino-5-(4-chlorophenyl)-1,5,6,7-tetrahydro pyrazolo[4,3-e]-thiopyrano[2,3-b] pyridine-6-carbonitrile. Compounds I a,b reacted with triethylorthformate in the presence of acetic anhydride in pyridine to give ethoxy methylene amino derivatives Va,b. Reaction of V with each of ammonium hydroxide, hydrazine hydrate and phenyl hydrazine in boiling ethanol gave 4-(4-chlorophenyl)-3,5-dicyano-5,6-dihydro-4*H*-thiopyran-2-yl) formamidine, 4,5,6,7-Tetrahydro-4-imino-5-aryl-3-amino-3*H*-thiopyrano[2,3-d]pyrimidine-6-carbonitrile, 4,5,6,7-Tetrahydro-4-imino-5-aryl-3-phenyl amine-3*H*-thiopyrano[2,3-d]pyrimidine-6-carbonitrile respectively. Reaction of compound III a,b with α-halo compounds, namely methyl iodide, phenacyl bromide, chloro acetone, monobromo malonitrile, and chloroacetonitrile in sodium ethoxide solution afforded S- alkylated compounds 4-amino-6,7-dihydro-2-alkylthio-5-aryl -5*H*-thiopyrano[2,3-d] pyrimidine-6-carbonitriles derivatives VI. Reaction of one product of VI(4-amino-5-(4-chlorophenyl)-2-(methylthio)-6,7-dihydro-5*H*-thiopyrano[2,3-d]-pyrimidine-6-carbonitrile) with hydrazine hydrate to yield 4-amino-2-hydrazinyl-6,7-dihydro-5-Aryl-5*H*-thiopyrano -[2,3-d]pyrimidine-6-carbonitrile derivatives (VII). To get a new series of expected biologically active compounds, it was of interest to condense hydrazine Compounds VII a,b with different aromatic aldehydes namely, benzaldehyde, p-chlorobenzaldehde, and p-methoxy benzaldehde in acetic acid to give the corresponding Schiff's bases. Compounds IIa, b reacted with a variety of α-halo compounds, namely methyl iodide , chloro acetonitrle, mono bromo malonitrile, chloro acetone, and phenacyl bromide in ethanol in presence of anhydrous potassium carbonate to give S-alkylated compounds (5-aryl-4,5,6,7-tetrahydro-2-(alkylthio)-4-thioxo-3*H*-thiopyrano[2,3-d]pyrimidine-6-carbonitrile derivatives). Reaction of 5-aryl-4,5,6,7-Tetrahydro-2-(methylthio)-4-thioxo-3*H*-thiopyrano[2,3-d] pyrimidine-6-carbonitrile derivatives (VIIIa,b) with hydrazine hydrate gave 2-hydrazinyl-4,5,6,7-tetrahydro-5-aryl-4-thioxo-3*H*-thiopyrano[2,3-d]pyrimidine-6-carbonitrile derivatives (IXa,b). Compound IXa,b was reacted with formic acid and ethylene glycol to give 6-aryl-5-thioxo-5,6,7,8-tetrahydro-1*H*-thiopyrano[2,3-d][1,2,4] triazolo[4,3-a]-pyrimidine-7-carbonitrile, and 6-Aryl-5-thioxo-5,6, 7,8-tetrahydro-1-*H*-thiopyrano[2,3-d]-[1,2,5]triazine[4,3-a]pyrimidine-7-carbonitrile respectively. Compounds VIIIa,b react with chloroacetonitrile afforded 5-(4-chlorophenyl)-3-(cyanomethyl)-4,5,6,7-tetrahydro-2-(methyl -thio)-4-thioxo-3*H*-thiopyrano[2,3-d] pyrimidine-6-carbonitrile Xa,b. Xa was reacted with hydrazine hydrate to yield 6-(4-chlorophenyl)-5-thioxo-5,6,7,8-tetrahydro-1-*H*-imidazo[1,2-a]thiopyran[2,3-d]pyrimidine-7-carbonitrile. Reaction of compound IIa,b with α-halocompounds, namly methyl iodide, phenacyl bromide, chloro acetone, monobromo malonitrile, and chloroacetonitrile in sodium ethoxide solution afforded S- alkylated compounds. Compounds IIa,b were reacted with two moles of alkyl halides in refluxing sodium ethoxide solution were by, the *S*,*S*-dialkyl derivatives. Reaction of compound IIa, b with mixture of chloroacetic acid and Benzaldehyde in one-pot reaction in the presences of acetic acid, acetic anhydride and sodium acetate to give 3-benzylidene-2-oxo-6-aryl-5-thioxo-2,3,5,6,7,8-hexahydrothiazolo [3,2-a] thiopyrano[2,3d] -pyrimidine-7-carbonitrile compounds. Most of new compounds were evaluated for their antimicrobial (*Staphylococcus aureus*, *Escherichia coli*) properties, and antifungal (*Aspergillus flavus*, *Candida albicans)*. Most of new compounds are antibacterial agents. All tested compounds are not antifungal except compound Ia.

The summary not more than 500 words