Abstract

Title: Synthesis and Antimicrobial Activity of Some New Heterocyclic Derivatives.

Keywords: 2-Aminobenzothiazol, dihydropyrimidins, thiazolidin-4-ones, *N*-Mannich bases, antimicrobial, antibiofilm.

Several new benzothiazole hybrids with other heterocyclic structures were synthesized in an attempt for exploring a new class of antibacterial, antifungal and antibiofilm agents. These derivatives include 2-(5-cyano-1,6-dihydro-6-oxo-4-arylpyrimidin-2-ylthio)-*N*-(6-substituted benzo [*d*] thiazol-2-yl)acetamide **IVa-n**, 2-imino-3-(6-substitutedbenzo[*d*]thiazol-2-yl)-5-(4-(un) substituted arylidenyl)thiazolidin-4-one **VIa-l** and 3-(6-Substitutedbenzo[*d*]thiazol-2-yl)-2-((*N*,*N*-disubstituted amino methyl)imino) thiazolidin-4-one **VIIa-f**. The target compounds were synthesized starting from 6-substitutedbenzo[*d*]thiazol-2-amine **Ia, Ib** and their structures were elucidated on the basis of elemental analyses and spectral data. These compounds were screened for their antibacterial activity against gram-positive bacteria (*B. subtilis*, *S. lutea* and *S. aureus*), gram-negative bacteria (*E. coli* ATCC 25922, *E. coli* ATCC 5087, *P. aeruginosa* and *P. vulgaris*) and antifungal activity against *C. albicans* through the sensitivity test using cup plate method. Minimum inhibitory concentration was measured for the only active compounds using agar dilution method. It was shown that the two classes incorporating the 2-imino-thiazolidin-4-one structure showed more antibacterial and antifungal activities and more pronounced MIC values than the class incorporating the dihydropyrimidinone. Additionally, the antibiofilm activity of the most active compounds **VIa, VIb, VIg, VIh, VIj, VIk, VIIc, VIId, VIIe** and **VIIf** as antifungals comparing to

fluconazole were screened against 2 pathogenic *Candida* isolates CA1 and CA2 using the fluconazole as the model system. Biofilm growth was monitored semiquantitatively by colorimetric assay using the crystal violet as indicator.

This thesis consists of the following parts:

1. Introduction:

In this section, a literature review about the various biological activities of benzothiazole derivatives was presented.

2. Rationale and Aim of the work:

It includes the research objectives and the rationale of the design of new compounds.

3. Discussion:

It dealt with the discussion of the experimental methods adopted for the synthesis of the designed compounds with a summarized data about the characterization of these new compounds .

4. Experimental:

In this part, the practical procedures adopted for the synthesis of the reported and new intermediates as well as the new final compounds were presented. In addition, their spectral and elemental micro analytical data are cited.

The following compounds were prepared.

***Reported intermediates:**

•*N*-(Benzo[*d*]thiazol-2-yl)-2-chloroacetamide **IIa.**

•2-Chloro-*N*-(6-methylbenzo[*d*]thiazol-2-yl) acetamide **IIb.**

• 1,2,3,4-Tetrahydro-4-oxo-6-phenyl-2-thioxopyrimidine-5-carbonitrile**IIIa.**

•6-(4-Chlorophenyl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile**IIIb.**

• 6-(4-Nitrophenyl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile **IIIc.**

•6-(4-Dimethylaminophenyl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile **IIId.**

•6-(4-Methoxyphenyl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile **IIIe.**

•6-(2-Chlorophenyl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile **IIIf.**

•6-(Furan-2-yl)-1,2,3,4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile **IIIg.**

•3-(Benzo[*d*]thiazol-2-yl)-2-iminothiazolidin-4-one **Va.**

•2-Imino-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one**Vb.**

***New final compounds (32 compounds):**

• *N*-(Benzo[*d*]thiazol-2-yl)-2-((5-cyano-6-oxo-4-phenyl-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVa.**

•*N*-(Benzo[d]thiazol-2-yl)-2-((4-(4-chlorophenyl)-5-cyano-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVb.**

• *N*-(Benzo[*d*]thiazol-2-yl)-2-((5-cyano-4-(4-nitrophenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVc.**

•N-(Benzo[d]thiazol-2-yl)-2-((5-cyano-4-(4- (dimethylaminophenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVd.**

•*N*-(Benzo[*d*]thiazol-2-yl)-2-((5-cyano-4-(4-methoxyphenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVe.**

• *N*-(Benzo[*d*]thiazol-2-yl)-2-((4-(2-chlorophenyl)-5-cyano-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVf.**

•*N*-(Benzo[*d*]thiazol-2-yl)-2-((5-cyano-4-(furan-2-yl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)acetamide **IVg.**

• 2-((5-Cyano-6-oxo-4-phenyl-1,6-dihydropyrimidin-2-yl)thio)-N-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVh.**

• 2-((4-(4-Chlorophenyl)-5-cyano-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVi.**

•2-((5-Cyano-4-(4-nitrophenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVj.**

•2-((5-Cyano-4-(4-(dimethylamino)phenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVk.**

•2-((5-Cyano-4-(4-methoxyphenyl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVl.**

•2-((4-(2-Chlorophenyl)-5-cyano-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVm.**

•2-((5-Cyano-4-(furan-2-yl)-6-oxo-1,6-dihydropyrimidin-2-yl)thio)-*N*-(6-methylbenzo[*d*]thiazol-2-yl)acetamide **IVn.**

•3-(Benzo[*d*]thiazol-2-yl)-5-benzylidene-2-iminothiazolidin-4-one **VIa.**

•3-(Benzo[*d*]thiazol-2-yl)-5-(4-chlorobenzylidene)-2-iminothiazolidin-4-one **VIb.**

•3-(Benzo[*d*]thiazol-2-yl)-2-imino-5-(4-nitrobenzylidene)thiazolidin-4-one **VIc.**

• 3-(Benzo[*d*]thiazol-2-yl)-5-(4-(dimethylamino)benzylidene)-2-iminothiazolidin-4-one **VId.**

•3-(Benzo[*d*]thiazol-2-yl)-2-imino-5-(4-methoxybenzylidene)thiazolidin-4-one **VIe.**

•3-(Benzo[*d*]thiazol-2-yl)-5-(2-chlorobenzylidene)-2-iminothiazolidin-4-one **VIf.**

•5-Benzylidene-2-imino-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIg.**

•5-(4-Chlorobenzylidene)-2-imino-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIh.**

•2-Imino-3-(6-methylbenzo[d]thiazol-2-yl)-5-(4-nitrobenzylidene)thiazolidin-4-one **VIi.**

•5-(4-(Dimethylamino)benzylidene)-2-imino-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIj.**

•2-Imino-5-(4-methoxybenzylidene)-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIk.**

•5-(2-Chlorobenzylidene)-2-imino-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIl.**

• 3-(Benzo[*d*]thiazol-2-yl)-2-((morpholinomethyl)imino)thiazolidin-4-one **VIIa.**

•3-(Benzo[*d*]thiazol-2-yl)-2-(((4-methylpiperazin-1-yl)methyl)imino)thiazolidin-4-one **VIIb.**

• 3-(Benzo[*d*]thiazol-2-yl)-2-(((dimethylamino)methyl)imino)thiazolidin-4-one **VIIc.**

• 3-(6-Methylbenzo[*d*]thiazol-2-yl)-2-((morpholinomethyl)imino)thiazolidin-4-one **VIId.**

• 3-(6-Methylbenzo[*d*]thiazol-2-yl)-2-(((4-methylpiperazin-1-yl)methyl)imino)thiazolidin-4-one **VIIe.**

•2-(((Dimethylamino)methyl)imino)-3-(6-methylbenzo[*d*]thiazol-2-yl)thiazolidin-4-one **VIIf.**

5.Microbial Screening:

The antimicrobial activity of the synthesized compounds was investigated against three gram-positive bacteria (*Staphylococcus aureus,Sarcina lutea* and *Bacillus subtilis),* four gram-negative bacteria (*Escherichia coli* ATCC 5087, *Escherichia coli* ATCC 25922, *Proteus vulgaris* and *Pseudomonas auroginosa)* using Ampicillin and Cefotaxime as standard drugs. In addition, the activity was tested against *Candida albicans* using fluconazole as standard drug. The compounds having good antifungal activity profile were subjected for antibiofilm screening using semi-quantitative screening method through microtiter plate reader using crystal violet as indicator.

6.References:

This part includes**(133)** references covering the period **(1960)** to the year **(2015)**.

7. Arabic summary.