ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

Synthesis of New Five-Membered Hetrocyclic Compounds from 2-Furfuryl Mercaptan Derivative and Evaluation of their Biological Activity

Luma S. Ahamed

Department of chemistry, College of Science, University of Baghdad, Baghdad, Iraq.

Abstract

Sixteen compounds were synthesized from 2- furfuryl mercaptan as starting material which was reacted with ethyl chloroacetate to produce 2-furfuryl mercaptan ester derivative. The later was reacted with hydrazine hydrate to produce hydrazide derivative(2)which was introduced in different synthetic methods by using either cyclization reactions or using different reagents to produce biheterocyclic systems(3-16).

Keyword: *Five-membered heterocycles, 2-furfuryl mercaptan, Biological activity.*

Introduction

Heterocyclic compounds are found in various forms and structures in medicines [1], many natural products, mostly vitamins [2], and biologically active compounds, including anti-HIV [3], anti-inflammatory [4], anti malarial 5, antiviral 6, fungicidal herbicidal, antitumor in synthetic pharmaceuticals they found as a key structural unit in artificial drugs 5 and Chemical materials used in agriculture [7-8].

There are a lot of heterocyclic compounds; especially those that contain five-membered heterocyclic with constitute a wide and differentiated group that have a wide range of biological activity spectrum [9-13]. There is a growing desire to develop the work of medicines in line with the ongoing developments of bacterial resistance to traditional antibiotics and as a result, there are ongoing attempts to create new compounds to avoid the mechanisms of resistance and they are undergoing biological study.

Experimental

^{1}HNMR and ^{13}C NMR spectrum (solvent DMSO-d6) was recorded on a 300 MHz spectrometer with TMS as internal standard in Al-Albayat University, Jordan. Melting points were determined on a Gallen-kamp MFB-600 melting point apparatus and are uncorrected. Analytical thin layer chromatography (TLC) was performed on plates precoated with silica gel (Merck 60 F254, 0.25 mm) and was visualized with ultraviolet light. The antimicrobial activity was performed in University of Baghdad, College of Science.

Preparation of (Furan-2-ylmethylsulfanyl)-acetic Acid Ethyl Ester (1)

Titled compounds were synthesized according to literature [14]. b.p 220; yield 90% IR (KBr): 1732(C=O), C-H "o.o.p"738; ^{1}HNMR (ppm):1.2 (t, 3H, CH_3), 3.1(s, 2H, SCH2CO), 3.9(s, 2H, furan-CH_2), 4.2(q, 2H, CH2-CH_3), 6.3-7.5(m, CH aromatic).

Preparation of (Furan- 2- ylmethyl sulfanyl) -acetic Acid Hydrazide (2)

Titled compounds were synthesized according to literature [15]. b.p 105 yield 82% IR (KBr) in cm^{-1}:3313 and 3211(NH), 1664(C=O), C-H "o.o.p"740, ^{1}HNMR (ppm): 3.8 (s, 2H, CH2-S), 3.9(s, 2H, furan-CH_2), 6.2-7.5 (m,CH aromatic), 3.1 (2H,NH_2) 7.9(s,1H,NH).

Synthesis of 1-(3, 5-Dimethyl-pyrazol-1-yl) -2-(furan-2-ylmethylsulfanyl) -ethanone (3)

To A mixture of 2 (0.0035 mole) in EtOH (50 ml), acetyl acetone (0.0035 mole) was added slowly, the reaction mixture was refluxed for 10h, then concentrated, cooled and the oil

product was extracted with hot hexane, evaporated to remove hexane to produce an oily yellow compound yield 60% IR (KBr) in cm^{-1}: 3313and 3211 (NH), 1726 (C=O), C-H "o.o.p"740.

Synthesis of 2-[2-(Furan-2-ylmethylsulfanyl) -acetyl] -5-methyl-2, 4-dihydro-pyrazol-3-one (4)

To A mixture of **2** (0.0035 mole) in EtOH (50 ml) ,ethyl acetoacetate (0.0035 mole) was added slowly ,the reaction mixture was refluxed for 10h, then it was concentrated, cooled and the solid product was filtered and recrystallized from acetone to give white needle crystal yield 82% , m. p 205-206 ^{O}C, IR (KBr):3176 (NH), 1662 (C=O), o.o.p"740 ; ^{1}HNMR (DMSO) (ppm): 2.5(s,3H,CH_3) 3.5 (s,2H,CH_2 of pyrazolone ring) 3.8(s, 2H,S-CH_2-CO), 3.9 (s, 2H,furan-C$\underline{H_2}$), 6.2-7.6(m, CH aromatic), 10.1 (s,1H,OH) ;^{13}CNMR (ppm): 164 (C=O), 155(C-OH)

Synthesis of -Amino-2-[2-(furan-2-ylmethylsulfanyl)-acetyl]-2,4-dihydro-pyrazol-3-one (5)

A mixture of compound (2) (0.015 mole), ethylcynoacetate (0.015mole) and few drops from pipredine in ethanol (50 ml) was refluxed for 13h then the reaction mixture was concentrated by heating than put in Petrie dish and wash by chloroform the precipitate was recrystallized from hexane yield 65% , m. p 180-183^{O}C , IR (KBr) cm^{-1}:3184 and 3234 (NH_2), 1662 (C=O), o.o.p"744 ; ^{1}HNMR (DMSO) (ppm):3.2 (s,2H,NH_2) 3.8(s, 2H,S-CH_2-CO), 3.9 (s, 2H, furan-C$\underline{H_2}$), 6.2-7.6(m, CH aromatic), 10.1 (s,1H,OH) ; 10.2 (s,1H,NH); ^{13}CNMR (ppm):171(C=O pyrazolidine), 164(C=O)

Synthesis of 5-(Furan-2-ylmethylsulfanylmethyl)-3H-[1, 3, 4] oxadiazole-2-thione (6)

Acid hydrazide (2) (1ml) was added slowly to a solution of potassium hydroxide(0.64 , 0.012 mole)in water (4ml)and ethanol (60ml) with stirring , then added CS_2 (10ml) slowly while stirring under cold condition (0-5C^{0}) after that the mixture was refluxed for 10h , the resulting solution was concentrated, the solid product was filtered and recrystallized from ethanol yield 72% yellow needle , m. p 263-265^{O}C, IR (KBr) in cm^{-1} :3344 (NH), 2729 (SH); ^{1}HNMR (DMSO) in ppm: 3.6(s, 2H,S-CH_2-CO), 3.8(s, 2H, furan-C$\underline{H_2}$), 6.2-7.6(m, CH aromatic), 12.8(SH);^{13}CNMR in ppm :185 (C=S), 176(C-SH).

Synthesis of 4-Amino-5-(furan-2-ylmethylsulfanylmethyl)-2, 4-dihydro-[1, 2, 4] triazole-3-thione (7)

A mixture of Compound (6) (0.01mole) , hydrazine hydrate(2.5ml , 98%) in ethanol (50ml) was reflux for 20h ,the formed solid was filtered and recrystallized from ethanol yield 72% , m. p 255-260^{O}C dec., IR(KBr) cm^{-1}:3207-3438 (NH and NH_2),2727(SH) ,1635(C=N)

Synthesis of (Furan-2-ylmethylsulfanyl)-acetic acid furan-2-ylmethylene-hydrazide (8)

A mixture of Compound (2) (0.015mole), furfural (0.015 mole) in ethanol (50ml) and a few drops of glacial acetic acid was refluxed for 20h. The reaction mixture was concentrated, the formed solid after cooling was filtered and recrystallized from ethanol: H2O (2:1). Yield 95%, m. p 95-93C^{O}, IR (KBr) in cm^{-1}:3147 (NH), 1641(C=N), 1666(C=O).

Synthesis of (Furan-2-ylmethylsulfanyl)-acetic Acid (1-furan-2-yl-ethylidene)-Hydrazide (9)

A mixture of Compound (2) (0.015mole), 2-acetylfuran (0.015 mole) in ethanol (50ml) and a few drops of glacial acetic acid was refluxed for 8h. The reaction mixture was concentrated, the formed solid after cooling was filtered and recrystallized from ethanol: H2O (2:1). yield 92% , m. p130-131 ^{O}C , IR(KBr):3228 (NH),1654(C=N) interferences with (C=O) ^{1}HNMR (DMSO) (in ppm):2.17 (s,3H,CH_3) 3.8(s, 2H,S-CH_2-CO), 3.9(s, 2H, furan-C$\underline{H_2}$), 6.3-8(m, CH aromatic), 10.4 (1H,NH); ^{13}CNMR (in ppm):11 (CH_3),13 (CH_3-C=N), 28 (furan-CH2) , 33(S-$\underline{CH_2}$CO),166(C=O)

Synthesis of Furan-2-ylmethylsulfanyl)-acetic acid N'-thiobenzoyl-hydrazide(10)

A mixture of Compound (2) (0.015mole), phenyl isothiocyanate (0.15mole) in benzene (50ml) was refluxed for (6 -8h). The formed solid after cooling over night was filtered and recrystallized from ethanol: H2O (2:1). IR(KBr)in cm^{-1}:3334-3170 (NH), 1674(C=O), 1276(C=S); ^{1}HNMR (DMSO) in ppm:3.4 (s,2H,CH2-CO), 3.9 (s,2H,furan-CH2), 9.3-10.3 (3NH and SH), 6.3-7.9(m,8H,Ar-H)

;^{13}CNMR in ppm:27 (furan-CH_2), 32(SCH_2-CO),155 (C=O), 168(C=S).

Synthesis of Biphenyl-4-carboxylic acid N'-[2-(furan-2-ylmethylsulfanyl)-acetyl]-hydrazide (11)

A mixture of Compound (2) (0.015mole), phenyl isocyanate(0.15mole) in benzene (50ml) was refluxed for (8h). The formed solid after cooling was filtered and recrystallized from a mixture of (acetone: ethanol) (2:3) yield 85%, m. p175-177^{O}C IR(KBr) in cm^{-1}:3390 and 3215(NH),1687 (C=O); ^{1}HNMR(DMSO) in ppm:2 (s,2H,CH2), 2.1(s,2H,CH2), 9(s,1H,NH), 9.75(s,1H,NH), 7.3-7.9 (m,12H,Ar-H) ;^{13}CNMR in ppm:,17 (furan-CH2), 25 (S$\underline{CH_2}$CO)153 (NHCONH) ,172(CONHNH).

Synthesis of Furan-2-ylmethylsulfanyl)-N-(4-oxo-2-phenylimino-thiazolidin-3-yl)-acetamide (12)

A mixture of Compound (10) (0.015mole), chloroacetic acid (0.015mole) was refluxed in ethanol (50ml) for 6h. The solid product after cooling was filtered and recrystallized from a mixture of (acetone: H2O) (2:2) yield 65% m. p 207-210 IR (KBr) in cm^{-1}:3234(NH), 1730(C=O), 1600(C=N)

Synthesis of (Furan-2-ylmethylsulfanyl)-acetic acid (4-oxo-3-phenyl-thiazolidin-2-ylidene)-hydrazide 13

A mixture of Compound (10) (0.015mole), ethylchloroacetate (0.015mole), and anhydrous potassium acetate (0.085mol) in ethanol (50ml) was refluxed for 6h. The solid product after cooling was filtered and recrystallized from a mixture of ethanol: H2O (2:1). Yield 70%, m. p253-255 ^{O}C IR (KBr) in cm^{-1}: 3234(NH), 1730(C=O) lactam ring, 1647(C=O) amid

Synthesis of [5-(Furan-2-ylmethylsulfanyl)-[1, 3, 4] thiadiazol-2-yl]-phenyl-amine 14

Concentrated of sulfuric acid (10ml) was added slowly (over a period of 30 min.) to a solution of Compound (10) (0.015mol) in ethanol (50ml) under cold condition with stirring, the stirring was continued at room temperature for additional 6h.

Than A reaction mixture was poured into ice/water with neutral by sodium bicarbonate. The solid product was filtered and recrystallized from a mixture of acetone: H_2O (2:1). Yield 86%, m. p228-230^{O}C dec. IR (KBr) in cm^{-1}:3238 and 3191 (NH), 1602.

Synthesis of 5-(Furan-2-ylmethylsulfanyl)-4-phenyl-2,4-dihydro-[1,2,4]triazole-3-thione 15

A mixture of Compound (10)(0.001mole)in 20% aq NaOH solution (15ml) was refluxed for 6h after complete the time of reaction, cooled , filtered. The filtrate was neutralized by addition HCl to PH=4 the solid product was filtered and recrystallized from a mixture of acetone: H2O (2:1).Yield 85% , m. p180-181 ^{O}C IR(KBr) in cm^{-1} :3101(NH), 2746(SH), 1242(C=S) ^{1}HNMR (DMSO) in ppm:3.5 (s,2H,CH2) 3.6(s,2H,CH2)6.1-7.5 (m,4H,Ar-H) and NH, 7.5(s,5H,ph-H),14 (s,1H,SH); ^{13}CNMR in ppm:25($\underline{CH2}$-pyrazole), 27(furan-$\underline{CH2}$),168(C=S).

Synthesis of 4-Biphenyl-4-yl-5-(furan-2-ylmethylsulfanyl)-2,4-dihydro-[1,2,4]triazol-3-one 16

The synthesis compound (16) as the same as the last method except using 10ml of 20% aq NaOH instead of 15ml of it and the solid product recrystallized from water . yield 82% , m. p 240^{O}C dec IR(KBr) in cm^{-1}: 3332 and3274(NH), 1722 (C=O); ^{1}HNMR (DMSO) in ppm:3.6 (s,4H,2CH2), 6.1-8.8 (m,12H,Ar-H), 12 (s,1H,OH), ^{13}CNMR in ppm:25(CH_2-pyrazole),26.9 (CH_2-furan),107-145 for (C-aromatic),150(C=O),154(C=N)

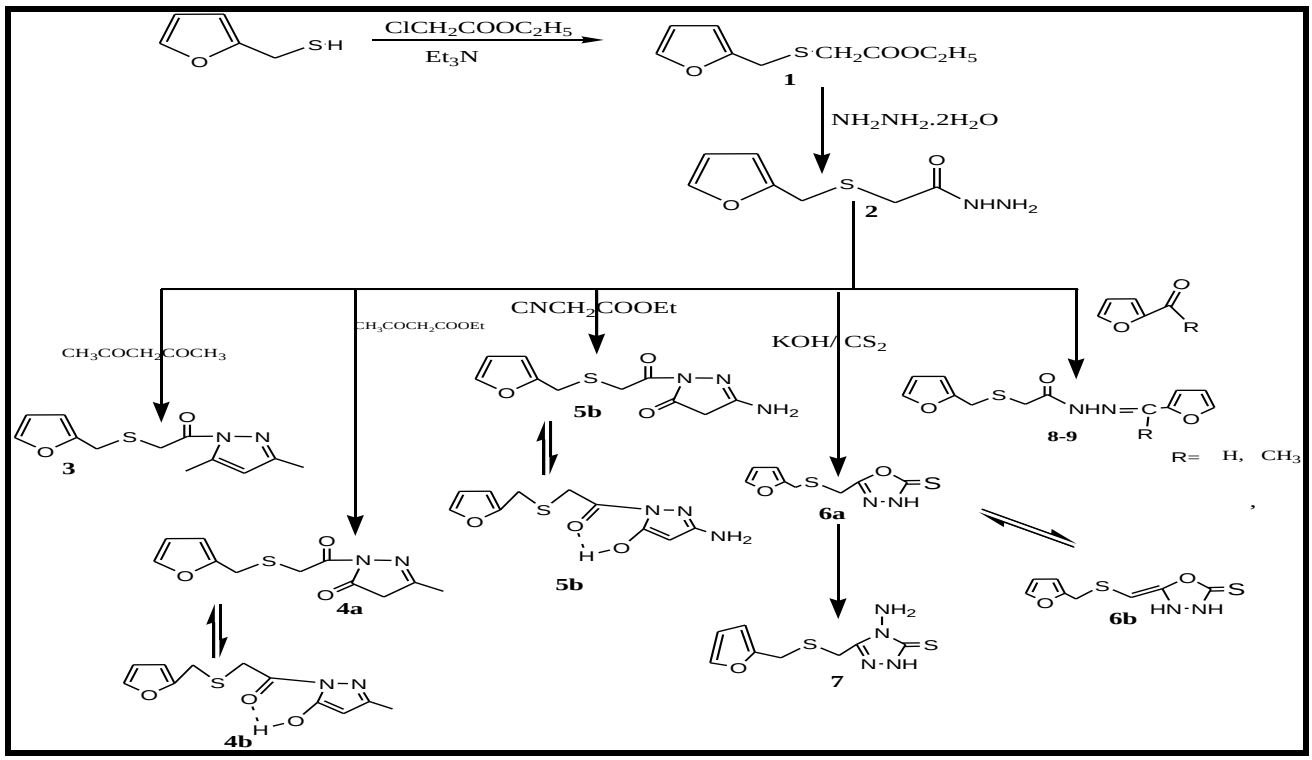
Results and Discussion

In the present work, (Furan-2-ylmethylsulfanyl)-acetic acid ethyl ester [1]was synthesized as starting material by reaction of furfural mercaptan with ethyl chloroacetate in the presence of trimethyl amine with heating then ester derivative treated with hydrazine hydrate to produce acid hydrizide [2] which was introduced many paths a way to produce new 5-membering heterocyclic compounds contain nitrogene and / or sulphur as shown in scheme 1, and scheme 2 the FTIR for compound [1] shows observed band at 1732 (C=O) [16], While ^{1}HNMR for the same compound showed triplet signal at 1.2ppm for CH_3 , singlet signal at 3.1 ppm for S-CH_2C=O group, singlet signal at 3.9 ppm for C=C-C$\underline{H_2}$-S,quertate at 4.2ppm for two protons $\underline{CH_2}$-CH_3, signals at (6.3-7.5) ppm for (C$\underline{H}$) aromatic protons while FTIR for the hydrazone compound [2] showed stretching bands at 3313 , 3211 and 3121 cm^{-1} due to v

NH and at 1664 cm^{-1} for v C=O stretch moreover in the ^{1}HNMR spectrum for the same compounds showed new signal at 3.1 ppm for NH_2 and signal at 7.9ppm for NH. Reaction of hydrazide 2 with acetyl acetone, ethylacetoacetate, and ethyl cyanoacetate to produce different pyrazole derivatives 3, 4 and 5.The IR of compound 3 showed disappearance of the absorption band of NH_2 and appearance of a strong absorption band at high frequency (1726 cm^{-1} (C=O)) comparing with hydrazide 2.

The IR of compound 4 showed band at 1662 cm^{-1} (C=O) its lowering frequency may be due to hydrogen bonding of hydroxylpyrazole 4b as shown in Scheme 1 .^{1}HNMR spectra for the same compound showed singlet signal at 2.5ppm for CH_3, singlet signal 3.5 ppm for CH_2 –pyrazolone ring, singlet signal at 3.8 ppm for S-CH_2 –CO, singlet signal at 3.9ppm CH_2 –furan ring, signals at (6.2-7.6ppm) for furan ring protons, and signal at 10.1ppm due to the hydroxyl group. ^{13}CNMR and ^{1}HNMR are a good evidence for the existence of compound 4 as its hydroxylpyrazole 4b as an equilibrium with 4a as shown in scheme 1 .The compound 5 showed the same results in IR,^{1}HNMR and ^{13}CNMR spectra , IR showed 1662 cm^{-1} (C=O), 3234, 3184 cm^{-1} (NH_2). ^{1}HNMR showed singlet signal at 3.2 ppm for $COC\underline{H_2}$-C-NH_2 , singlet signal at 3.5 ppm for two protons of NH_2 , singlet signal at 3.8ppm for (S-CH_2-CO) , singlet signal at 3.9ppm for furan-$\underline{CH_2}$, singlet signal at 10ppm for hydroxyl group ,^{13}CNMR showed signal at 164 and 171 ppm for C=O of CH_2CO and (C=O) of pyrazolone ring respectively the hydrogen bond may confirm the structure to form as hydroxylpyrazole 5b as an equilibrium with 4a as shown in Scheme1.

FTIR spectrum for Compound 6 showed bands at 3344 and 1635cm^{-1} for NH, and C=N, respectively, while ^{1}HNMR showed singlet signal at 3.6 ppm for two protons of (CH_2C=N) ,and singlet signal at 12.9 ppm for the proton of SH ^{13}CNMR showed 176 and 185 ppm for HS-C=N and C=S respectively. When compound 6 was treated with hydrazine hydrate in ethanol absolute gave amino derivative 7, FTIR spectrum for Compound 7 showed absorption bands at 3207 and 3342(NH_2), 3352 (NH_2) ,1635(C=N) and 2727 Cm^{-1} (SH).

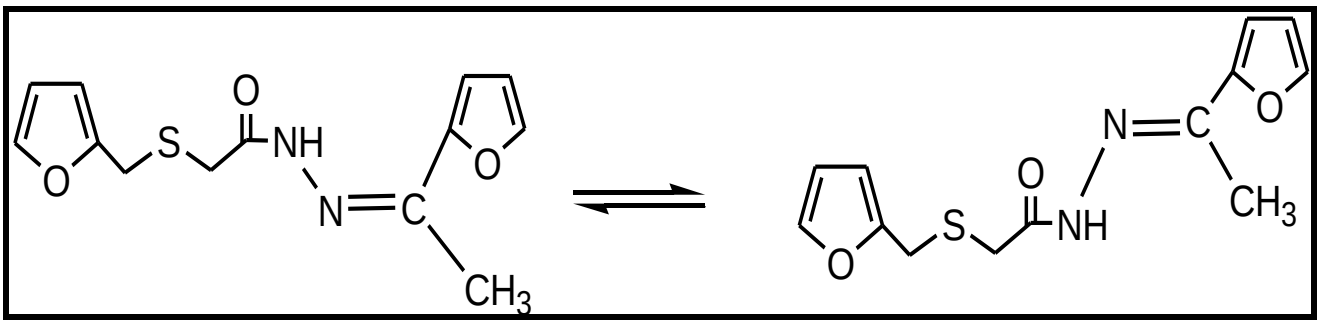


Scheme1:

When acid hydrazide was treated with different carbonyl compounds in ethanol absolute with a few drops of glacial acetic acid gave Schiff base derivatives 8 and 9. FTIR spectrum for Compound 8 showed bands at 3147 for (NH), 1641 (C=N), and 1666 (C=O amid), while compound 9 showed at 3228 for (NH), and 1654 (C=O amid).

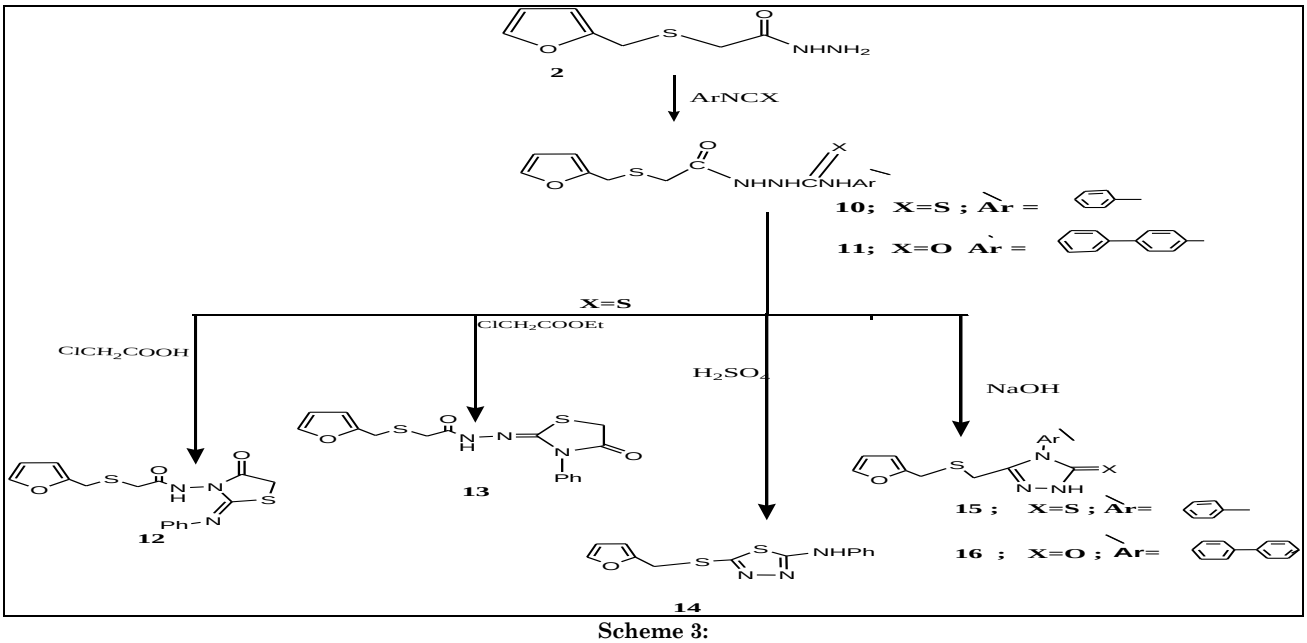
^{1}HNMR for the same compound showed singlet signal at 2.17 ppm for protons of (CH_3) group, singlet signal at 3.9 for two

protons of (furan-CH_2) , singlet signal at 3.8 for two protons of (S-CH_2)group, signals at (6.3-8)ppm for aromatic protons ,and two signals at 10.4 ppm for (N-H) may be due to totuamerisium structures as shown in Scheme 2 .



Scheme 2:

^{13}CNMR spectra showed new signal at 11ppm for CH_3 group. When acid hydrazide 2 was treated with phenylisothiocyanate and phenylisocyanate to produce compounds 10 and 11 respectively as shown in Schem3.FTIR spectral data of compound 10 showed absorption bands for (N-H) at 3334-3170, C=O at 1674, C=S at 1276 cm^{-1} and absent of the absorption band for SH.The ^{1}HNMR spectrum for the same compound showed signals at 9.3-10.3 ppm due to NH and SH while ^{13}CNMR spectrum showed signal at155ppm for carbon of carbonyl amide group and 168ppm for (C=S). The FTIR spectral data of compound 11 showed the absorption band for NH at 3390and 3215 cm^{-1} and (C=O) amide at 1687 cm^{-1} The ^{1}HNMR spectrum for the same compound showed signals at 9 and 9.75 ppm for NH groups while ^{13}CNMR spectrum showed signals at 153 and 148ppm for (C=O) amide groups. Cyclization of thiosemicarbazide derivative was obtained when treated compound 10 with chloroacetic acid to produce thiazolidinone derivative12. The FTIR spectral data of compound 12 showed the absorption band for NH at 3234 cm^{-1}, and at 1730 for C=O of lactam ring. When thiosemicarbazide 10 was treated with chloro ethylacetate in ethanol in the present of anhydrous potassium acetate to produce thiazolidinone derivative 13 FTIR spectral data of compound 13 showed absorption bands for (N-H) at 3234, (C=O) at 1730 for thiazolidinone ring and (C=O) amide at 1647 cm^{-1} . While the reaction of thiosemicarbazide 10 with cold H_2SO_4 at high concentration produced [5-(Furan-2-ylmethylsulfanyl)-[1, 3, 4] thiadiazol-2-yl]-phenyl-amine 14.The reaction involved attacking carbonyl group by the C=S sulfur atom. FTIR spectral data of compound 14 showed disappearing absorption band of the carbonyl group and appearing absorption bands for NH at 3238 and 3436 cm^{-1}.



Scheme 3:

Cyclization of compounds 10 and 11 by treating them with NaOH to produce the corresponding compound 5-(Furan-2-ylmethylsulfanyl)-4-phenyl-2,4-dihydro-[1,2,4] triazole-3-thione **15** and 4-Biphenyl-4-yl-5-(furan-2-ylmethylsulfanyl)-2,4-dihydro-[1,2,4] triazol-3-one**16** respectively.

FTIR spectral data (in cm $^{-1}$) of compound 15 showed the absorption band for NH at 3101 , SH at 2746 and C=S at 1242 ^{1}HNMR spectrum for the same compound showed signal at 14ppm due to SH while. ^{13}CNMR spectrum showed signal at 168 ppm for N=C-SH.

FTIR spectral data of compound 16 showed absorption bands at 3332 and 3274 for NH, and for C=O at 1722 cm^{-1} .^{1}HNMR spectrum for the same compound showed signal at 11.9 ppm due to O-H while ^{13}CNMR spectrum showed signals at 156 ppm due to N=C-OH and at 152 ppm for N=C-N.

Anti-biological Activity

The synthesized compounds were screened against two types of bacteria, gram positive Staphyloccous aureus and gram negative Escherichia Coli using the ager well-diffusion method in DMSO as solvent each type of bacteria were incubated for 16 hrs.

At 37 ^{o}C the results of biological activity of our synthesized compound are shown in Table as zone of inhibition (mm) and the concentration used is 100µg/ ml of DMSO. The results obtained showed that the triazole derivative 7 was the most active compounds against Staphylocous. aureus without any active against E. Coli.

While the triazole 16 was a good active against Staphyloccous aureus only, but triazole 15 showed biological activity against two types of bacteria. Two pyrazoles (3 and 4) showed good active compounds toward the two types of bacteria while pyrazole 5 show a good activity against only Staphyloccous aureus. In addition the thiosemicarbazide derivate 11, which has no other heterocyclic ring, had shown no biological activity. Other results are shown in Table 1and Fig.1-2.

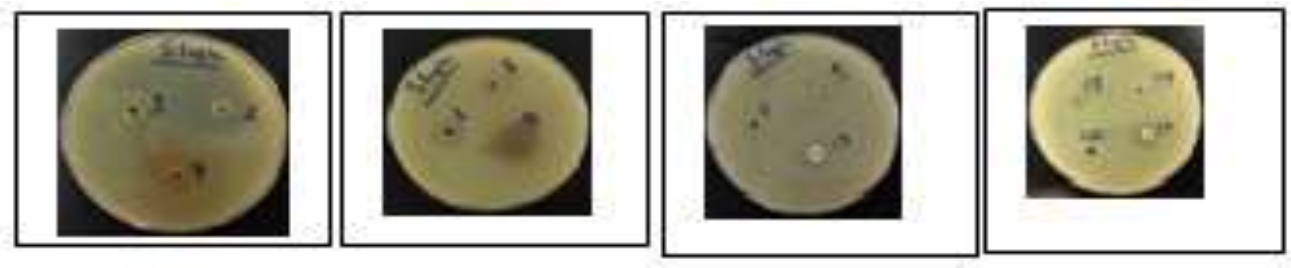


Fig. 1: Antimicrobiak activity of selected compounds against S. aureus aureus

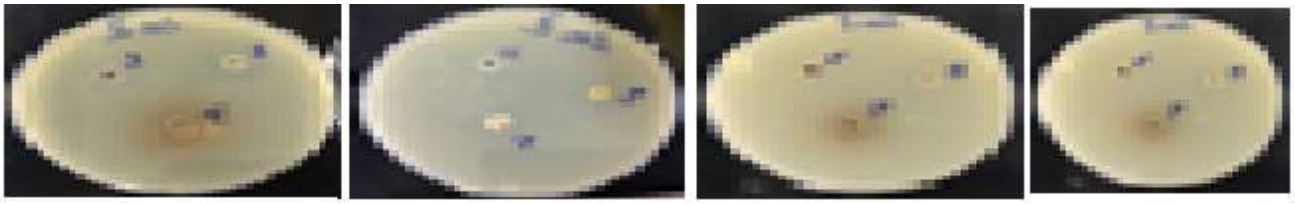


Fig.2: Antimicrobial activity of selected compounds against E. coli

Table 1: Antimicrobiak activity of selected compounds

compounds No.	*S. aureus*	E. Coli(mm)
2	31	14
3	15	11
4	9	14
5	16	-
6	12	-
7	21	-
9	14	-
11	-	-
13	14	-
14	7	8
15	11	10
16	14	-
diclofenac	10	18
Control DMSO	7	-

Conclusion

New heterocyclic compounds were synthesized starting from 2-furfuryl mercaptan; the isolated compounds were tested against two types of bacteria *Staphylococcus. aureus* and Escherichia .Col. Most compounds shows more active against S.aureus than the stander drug (diclofenac).

References

1. Pedro Martins, João Jesus, Sofia Santos, Luis R Raposo, Catarina Roma-Rodrigues, Pedro Viana Baptista, Alexandra R Fernandes (2015) Heterocyclic Anticancer Compounds: Recent Advances and the Paradigm Shift towards the Use of Nanomedicine's Tool Box Molecules, 20:16852-16891.
2. Rajiv Dua, Suman Shrivastava, 1 1 1 SK Sonwane, 2SK Srivastava (2011) Pharmacological Significance of Synthetic Heterocycles Scaffold: A Review Advances in Biological Research, 5(3): 120-144.
3. Luis M Bedoya, Esther del Olmo, Rocıo Sancho,Bianca Barboza, Manuela Beltran, Ana E Garcıa-Cadenas, Sonsoles Sanchez-Palomino, Jose L Lopez-Perez, Eduardo Munoz, Arturo San Felicianob, Jose Alcamı (2006) Anti-HIV activity of stilbene-related heterocyclic compounds Bioorganic & Medicinal Chemistry Letters 16: 4075-4079.
4. Preeti Rani, VK Srivastava, Ashok Kumar (2004) Synthesis and anti inflammatory activity of heterocyclic indole derivatives European Journal of Medicinal Chemistry 39: 449-452.
5. Jean Guillon, Anita Cohen, Nassima Meriem Gueddouda, Rabindra Nath Das, Stéphane Moreau, Luisa Ronga, Solène Savrimoutou, Louise Basmaciyan, Alix Monnier, Myriam Monget, Sandra Rubio, Timothée Garnerin, Nadine Azas, Jean-Louis Mergny, Catherine Mullié Pascal Sonnet (2017) Design, synthesis and antimalarial activity of novel bis{N-[(pyrrolo[1,2-a]quinoxalin-4-yl)benzyl]-3-aminopropyl}amine derivatives Journal of Enzyme Inhibition and Medicinal Chemistry, 32 (1): 547-563.
6. Ghada S, Hassana Ali, A El-Emama Laila, M GadbAlaa, Eldin MBarghashc Synthesis, antimicrobial and antiviral testing of some new 1-adamantyl analogues, 18 (3): 111-178.
7. Ahmed Abdou O Abeed, Mohamed Salah K Youssef, Rehab Hegazy (2017) Synthesis, Anti-Diabetic and Renoprotective Activity of Some New Benzazole, Thiazolidin-4-one and Azetidin-2-one Derivatives J. Braz. Chem. Soc., 28 (11): 2054-2063.
8. kaav international journal of science, engineering & technology(the study of amide and importance of biologically agrochemicals) KIJSET/JUL-SEP2016/VOL-3/Iss-3/A3 pp.12-15
9. Jialong Sun, Yuanming Zhou (2015) Synthesis and Antifungal Activity of the Derivatives of Novel Pyrazole Carboxamide and Isoxazolol Pyrazole Carboxylate Molecules, 20: 4383-4394.
10. Yehia Abdel-Galele Mahmoud, Fawy M, Abd El Latif, Amr A Amra, Osman A Osman (2018) Synthesis of New Heterocyclic Compounds with Biological Activity against Pathogenic Microbes in the Albaha Area Yehia Abdel-Galele Mahmoud. Biomed J. Sci. & Tech. Res., 2: 5.
11. Suresh Kumar, Sandhya Bawa, Sushma Drabu, Rajiv Kumar1, Himanshu Gupta (2009) Biological Activities of Pyrazoline Derivatives -A Recent Development Recent Patents on Anti-Infective Drug Discovery, 4: 154-163.
12. Rana Abid Ali, Luma S Ahamed, Zena G Alrekabi (2018) J. Pharm. Sci. & Res. Synthesis of New Nucleoside Analogues from 3, 5-Disubstituted Pyrazoline, 10(4): 705-710.
13. Mousa Al-Smadi, Fouad Al-Momani (2008) Synthesis, Characterization and Antimicrobial Activity of New 1, 2, 3-Selenadiazoles Molecules, 13: 2740-2749.
14. PB Mohitea, VH Bhaskar (2011) Synthesis and evaluation of antimicrobial activity of novel 1,3,4-oxadiazole derivatives, Orbital Elec. J. Chem., 3(2): 117-124.
15. Redha I Al-Bayati, Mohammed R Ahamad, Luma S Ahamed (2015) Synthesis and Biological Activity Investigation of Some Quinoline-2-One, Derivatives. American Journal of Organic Chemistry, 5(4): 125-135.
16. Silverstein R, Webster F, Kiemle D (2005) Spectroscopic identification of organic compounds, 7th Ed., John Wiley & Sons, Inc., USA.

***Corresponding Author Email:** *lumasami71@yahoo.com*

