ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

Synthesis of New Heterocyclic Derivatives from Thiophenol and Evaluation their Biological Activity

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Abstract

S-Chloroacetyl thiophenol (A) was synthesized by reaction of thiophenol with chloroacetyl chlorid, then the product (A) was reacted with hydrazine hydrate to give hydrazide derivative (B), which was introduced in different synthetic methods to produce either Schiff bases derivatives or to produce heterocyclic compounds. All compounds were confirmed by their melting point, FT-IR spectra, ^{1}H-NMR, ^{13}C-NMR spectrum and studying the possibility for their application as antibacterial and antifungal agents to some of them.

Keywords: *Thiopohenol, Hydrazen hydrate, Schiff bases.*

Introduction

Thiols and mercaptans are organosulfur compounds that contain a sulfur-hydrogen bond and similar to the hydroxyl organization (-OH) of alcohol, but the chemical differences between oxygen and sulfur give the group its specific lines [1].

Thiol compounds play key roles in biological systems, where there are three mercapto biomolecules that maintaining on the biological systems. In which, cysteine (Cys), homocysteine (Hcy) and glutathione (GSH) have similar structures [2]. The practical organization of thiol is essential for protein shape due to its capability to create a disulfide bond with a 2d cysteine, and is frequently concerned in the active website of the enzyme.

Those compounds may be used as constructing blocks for natural syntheses and are useful in syntheses, including redox chemistry, alkyls, Michael additions, and cross-coupling reaction [3]. Cyclic organic compound containing all carbon atoms in ring formation is referred to as a carbocyclic compound. If at least on atom other than carbon forms a part of the ring system is designated as heterocyclic compound [4].

Most common heterocyclic are those having five or six-membered rings and containing heteroatoms of nitrogen (N), oxygen (O) or sulfur (S). The best known of the simple heterocyclic compounds are pyridine, pyrrole, furan, and thiophene [5]. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways [6]. A number of heterocyclic derivatives containing nitrogen and sulfur atom serve as a unique and versatile scaffolds for experimental drug design [7].

Heterocyclic compounds are also finding an increasing use as intermediate in organic synthesis [8]. Chlorophyll and them, which are derivatives of porphyrin ring system are the components required for the photosynthesis and for oxygen transport in higher plants and in animal. Essential diet ingredients such as thiamin (vitamin B1), riboflavin (B2), pyridoxol (vitamin B6), nicotinamide (vitamin B3) and ascorbic acid (vitamin C) are heterocyclic compounds [9].

Chemicals and Instruments

Chemicals

All chemicals were purchased from Fluke and BDH.

Instruments

- Melting point were recorded using Gallenkamp capillary melting point apparatus.
- FT-IR spectra were recorded using KBr disc on shimadzu FT-IR8400 Fourier Transform Infrared spectrophotometer.
- Some of the prepared compounds were characterized by ^{1}H-NMR and ^{13}C-HNMR spectra that recorded on nuclear magnetic resonance in 600 MHz (Laboratory of Isfahan University) and DMSO as solvent.
- The biological activity was performed by the Central Environmental Laboratory University of Baghdad (Anti-bacteria) and Research Laboratory of Environment and Pollution College of Science University of Al-Qadisiyah (Anti-fungal).

Experimental

Synthesis of S-Chloroacetyl thiophenol [A] [10]

A mixture of thiophenol (5ml) (0.05mol.), dry benzene (5ml) and tert-amine (tri-methylamine) (2.5ml) was stirred for (20min) then added (5.5ml) (0.05mol.) of chloroacetyl chloride gradually, the mixture refluxed for (8hr) on water bath (70-80) C^0. The oily product was obtained after remove of the solvent.

Synthesis of S- (acetohydrazide) thiophenol [B] [11]

Dissolved (10ml) (0.054mol.) of S-chloroacetyl thiophenol [A] in (15ml) of dry chloroform, then add (2.7ml) (0.054mol.) hydrazine hydrate gradually with continuous stirring. The mixture stirred for (10hr) at room temperature. The final product was dried then recrystallized from ethanol.

Synthesis of S-[N-substiuted benzylidine acetohydrazide] thiophenol [1-12] [12]

Equimolar quantities (0.5 gm.) (0.003mol.) from S-(acetohydrazide) thiophenol [B] and aromatic aldehyde (0.003mol.) in (20ml) of absolute ethanol and (3-4) drops of glacial acetic acid were refluxed for (6hr) at (50-60) C^0. The hot product decanted on cold water then filtered and washed by distilled water and the solid product was recrystallized from ethanol. The physical properties of compounds [1-12] are listed in Table (1).

Synthesis of S-(aceto phenyl semi carbazide) thiophenol [13] [13]

To dissolved solution of S-(acetohydrazide) thiophenol [B] (5 gm.) (0. 03 mol.) in (15 ml) of absolute ethanol, (3.4 ml) (0.03 mol.) of isophenylcynate was added gradually with continuous stirring. The mixture was stirred for (5hr) at room temperature and the product dried then recrystallized from benzene. The physical properties of compound [13] are listed in Table (1).

Synthesis of S-(4-phenyl-1, 2, 4-triazine-3-one) thiophenol [14]

Dissolve (0.5gm.) (0.002mol.) of S-(aceto phenyl semi carbazide) thiophenol [13] in (10ml) of absolute ethanol, then add (1gm.) of sodium hydroxide (NaOH) and (0.04 gm.) $ZnCl_2$, the mixture was refluxed at high temperature for (5hr).Then dried the product. The physical properties of compound [14] are listed in Table (1).

Synthesis of S-(4-phenyl-1,2,4-triazine-3-substituted) thiophenol [15, 16] and S-(4-phenyl-2-N-substituted 1,2,4-triazine-3-one) thiophenol [17-19] [14]

Add (0.056 gm.) from potassium hydroxide (KOH) during (20 min) to a stirred dissolved solution of (0.3 gm.) (0.001mol.) S-(4-phenyl-1, 2, 4-triazine-3-one) thiophenol [14] in (10 ml) ethanol at ($50C^0$), then (0.001 mol.) of alkyl halides was added drop wise and the mixture was refluxed for (5hr). The reaction mixture was filtered, cooled, and poured onto cold water then the resulting aqueous layer was extracted with chloroform (3×10 ml). The combined chloroform extracts was evaporated to give the desired product that recrystallized from dry benzene. The physical properties of compounds [15-19] are listed in Table (1).

Synthesis of S-(N-aceto phenyl semi thiocarbazide) thiophenol [20] [13]

The same procedure that used to prepare S-(aceto phenyl semi carbazide) thiophenol [13] compound but using isothiophenylcynate. The physical properties of compound [20] listed in Table (1).

Synthesis S-(4-phenyl-1, 2, 4-triazine-3-thion) thiophenol [21]

The same procedure that used to prepare S-(4-phenyl-1, 2, 4-triazine-3-one) thiophenol [14] compound but using (0.5gm.) of NaOH.

The physical properties of compound [21] are listed in Table (1).

Synthesis of S-(4-phenyl-2-N-substituted-1, 2, 4-triazin-3-thion) thiophenol [22, 23] and S-(4-phenyl-1, 2, 4-triazine-3-substituted) thiophenol [24-26] [14]

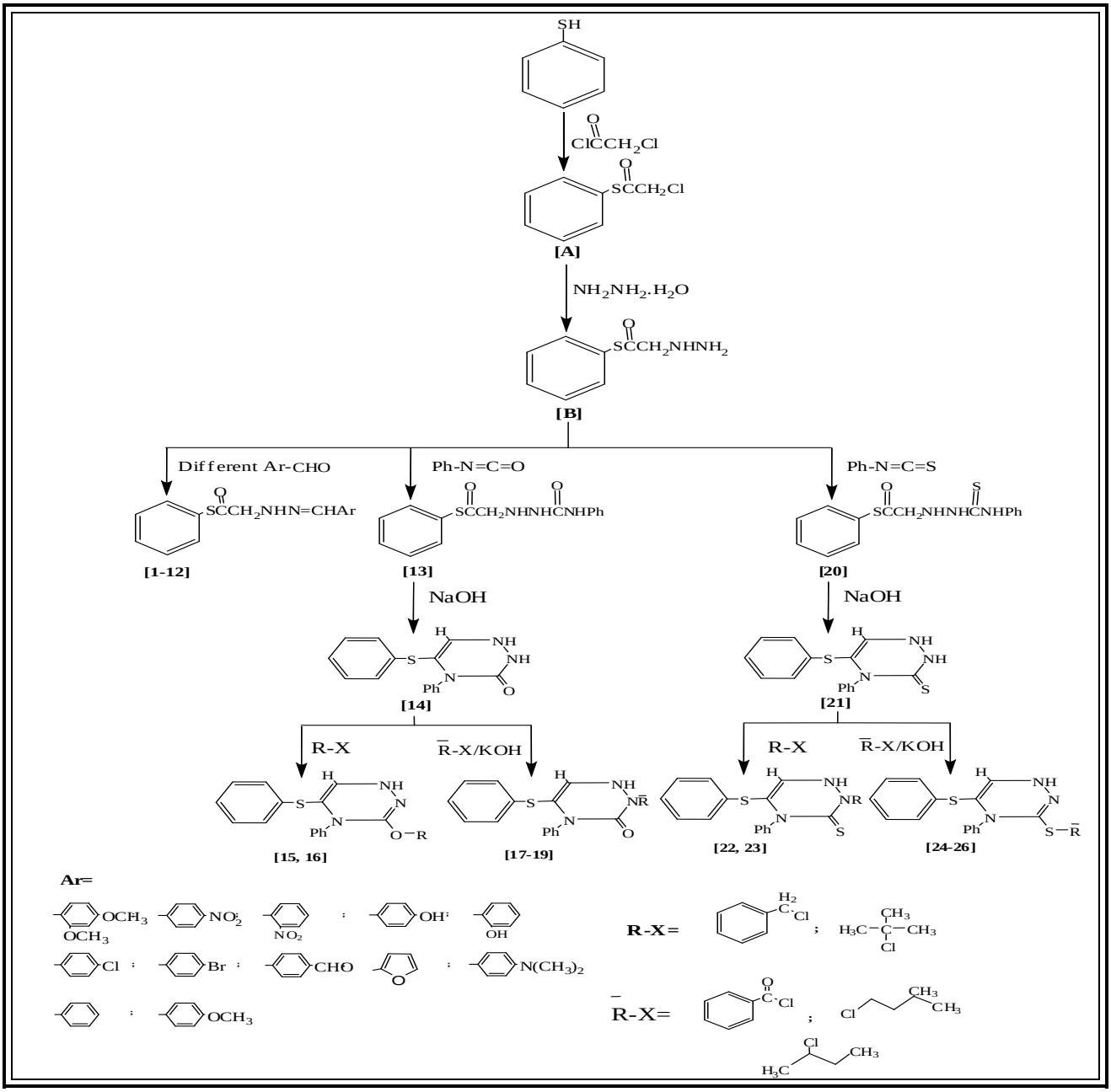
The same procedure that used to prepare compounds [15-19]. The physical properties of compounds [22-26] are listed in Table (1).

Biological Activity

Several prepared compounds were tested for their in vitro growth inhibitory activity against *Escherichia coli, Staphylococcus aurus, Klebsiella pneumonia* and *Staphylococcus epidermidis* bacteria and *Aspergillus* fungal by applying cup plate method using nutrient agar medium and dimethyl sulfoxide that used as a sample solution [15, 16].The test organisms were first cultured in nutrient broth and incubated for (24) hrs at 37 ^{0}C and then freshly prepared bacterial cells were spread onto the nutrient agar. The tested compounds were previously dissolved in dimethyl sulfoxide then (0.1 mL) of each compound (known concentration) was added in the cups and the petri dishes were subsequently incubated at 37 ^{0}C for 24 hrs, Inhibition zone produced each compound was measured in (mm) and all results are listed in Tables (5 and 6).

Results and Discussion

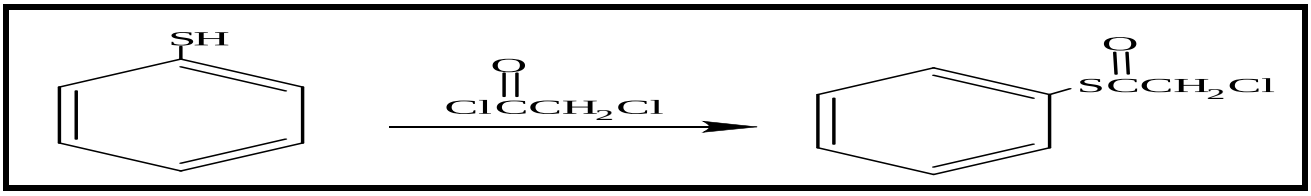
This work includes synthesis a new Schiff bases and heterocyclic derivatives from thiophenol as shown in Scheme (1).



Scheme 1:

Synthesis of S-chloroacetyl thiophenol [A]

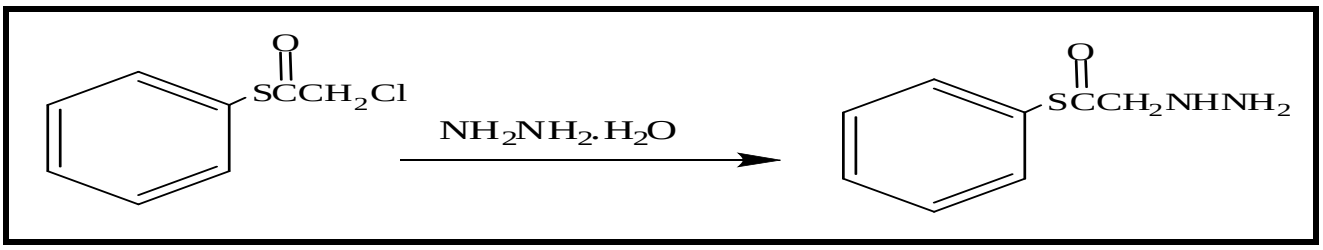
The reaction of thiophenol with chloroacetyl chloride in alkali medium will produce S-chloroacetyl thiophenol [A] compound as shown in Equation (3.1).Light yellow, Oily, yield (95 %). FT-IR spectrum of compound (A) showed the appearance of characteristic absorption bands at (790) cm^{-1} belong to v (C-Cl), (2939) cm^{-1} belong to v (C-H) aliphatic, (1691) cm^{-1} belong to v (C=O) and disappearance of the absorption band at (2567) cm^{-1} due to v (S-H).



Equation

Synthesis of S- (acetohydrazide) thiophenol [B]

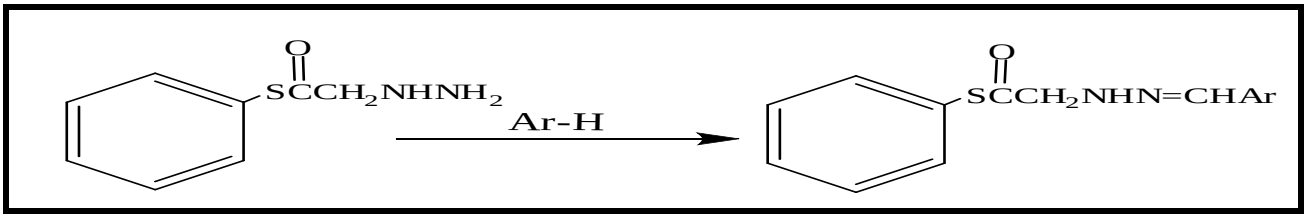
The treatment of compound [A] with hydrazine hydrate in dry chloroform will produced the main important compound [B] as shown in Equation (3.1). Dark yellow, M.P (128-130) C^0 yield (885). %). FT-IR spectrum of compound (B) showed the appearance of characteristic an absorption bands at (3317, 3465) cm^{-1} belong to v (NH_2), (3244) cm^{-1} belong to v (NH), (1650) cm^{-1} belong to v (C=O) and disappearance of the absorption band at (790) cm^{-1} due to v(C-Cl). ^{1}H-NMR and ^{13}C-NMR see in Tables (3), (4) and Figures (1, 2 and 11).



Equation

Synthesis of S-[N-substiuted benzylidine acetohydrazide] thiophenol [1-12]

Schiff base derivatives [1-12] were prepared by condensation reaction between S-(acetohydrazide) thiophenol [B] and different substituted aromatic aldehyde in present of glacial acetic acid as shown in Equation (3.3). Physical properties of these compounds (1-12) are listed in Table (1). FT-IR spectrum of compounds [1-12] showed the appearance of characteristic bands at (1668-1602) cm^{-1} belong to v (C=N), (1697-1633) cm^{-1} belong to v(C=O). All other details of FT-IR spectral data of compounds (1-12) are listed in Table (2) and of compounds (2, 12) shown in Figures (12, 13). ^{1}HNMR, ^{13}C-NMR of compounds (2, 12) sees in Tables (3), (4) and Figures (3-6).

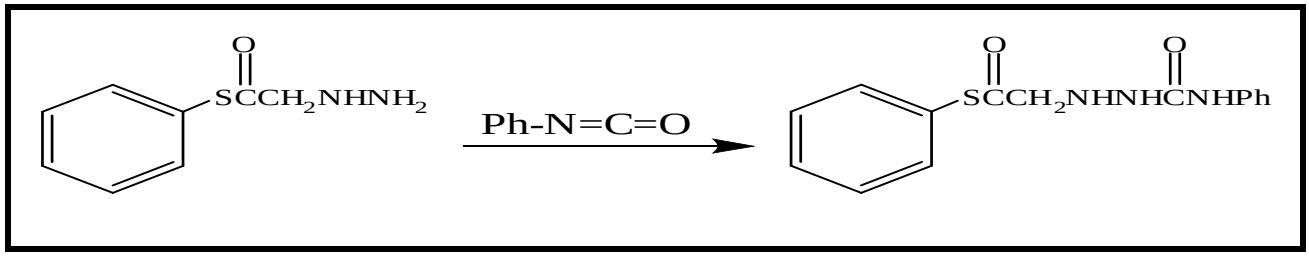


Equation

Synthesis of S-(aceto phenyl semicarbazide) thiophenol [13]

The reaction of compound [B] with phenylisocyanate in absolute ethanol will produce compound [13] as shown in Equation (3.4). Physical properties of compound (13) are listed in Table (1). FT-IR spectrum of

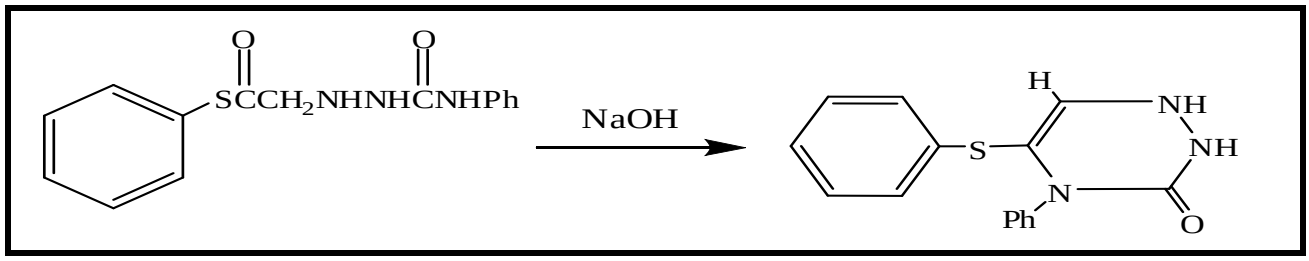
compound [13] showed the appearance of characteristic bands at (3313, 3203) cm^{-1} belong to v (NH), (1704) cm^{-1} belong to v(C=O) thioester, (1672) cm^{-1} belong to v(C=O) amide. All other details of FT-IR spectral data of compound (13) are listed in Table (2) and Figure (14). ^{1}HNMR, ^{13}C-NMR sees in Tables (3), (4) and Figures (7, 8).



Equation

Synthesis of S-(4-phenyl-1, 2, 4-triazine-3-one) thiophenol [14]

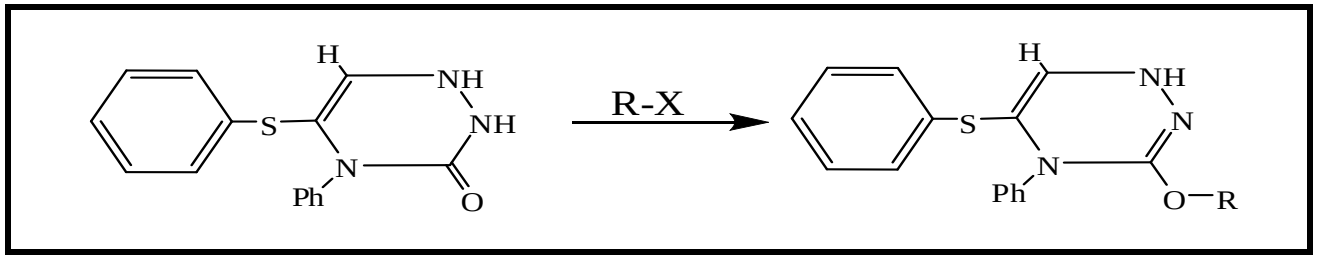
The treatment of compound [13] with NaOH affords intramolecular cyclization to give compound [14] as shown in Equation (3.5). Mechanism of reaction involved nucleophilic substitutions lead to intramolecular cyclization by S_N1 mechanism. Physical properties of compound [14] are listed in Table (1). FT-IR spectrum of compound [14] showed the appearance of characteristic bands at (3402, 3382) cm^{-1} belong to v (NH), (1618) cm^{-1} belong to v(C=O) imide(I) and disappearance band at (1704) cm^{-1} belong to v(C=O) thioester . All other details of FT-IR spectral data of compound (14) are listed in Table (2) and ^{1}HNMR spectral data sees in Table (3).



Equation

Synthesis of S-(4-phenyl-1, 2, 4-triazine-3-substituted) thiophenol [15, 16]

The cyclic compound [14] used to prepare compounds [15, 16] by the reaction with different alkyl halide in basic medium as shown in Equation (3.6). This reaction occurs under S_N1 mechanism. Physical properties of compounds (15, 16) are listed in Table (1). FT-IR spectrum of compound [15, 16] showed the appearance of characteristic bands at (1627, 1641) cm^{-1} belong to v (C=N), (1598, 1552) cm^{-1} belong to (C=C) alkene, (3386, 3367) cm^{-1} belong to (NH). All other details of FT-IR spectral data of compounds (15, 16) are listed in Table (2) and ^{1}HNMR spectral data of compound (15) sees in Table (3).



Equation

S-(4-phenyl-2-N-substituted 1, 2, 4-triazine-3-one) thiophenol [17-19]

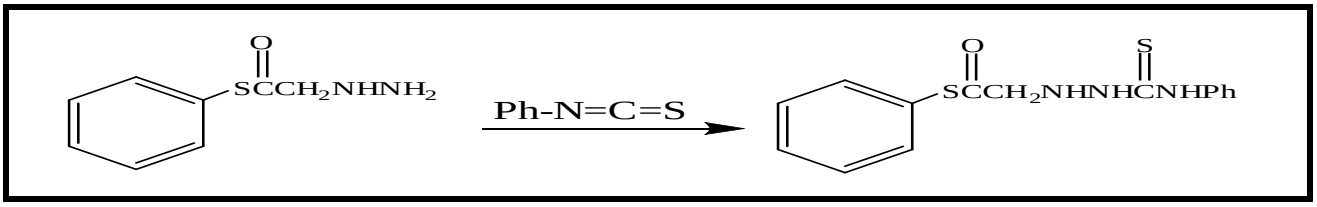
Alkylation reaction to compound [14] with different alkyl halides under basic conditions gives different derivatives [17-19] as shown in Equation (3.7). This reaction occurs under S_N2 mechanism. Physical properties of compounds (17-19) are listed in Table (1). FT-IR spectrum of compounds [17-19] showed appearance of characteristic bands at (1687-1620) cm^{-1} belong to v(C=O), (1595-1581) cm^{-1} belong to v(C=C) alkene and (3409-3068) cm^{-1}

belong to (NH). All other details of FT-IR spectral data of compounds (17-19) are listed in Table (2).

Equation

S-(N-aceto Phenyl Semi thiocarbazide) thiophenol [20]

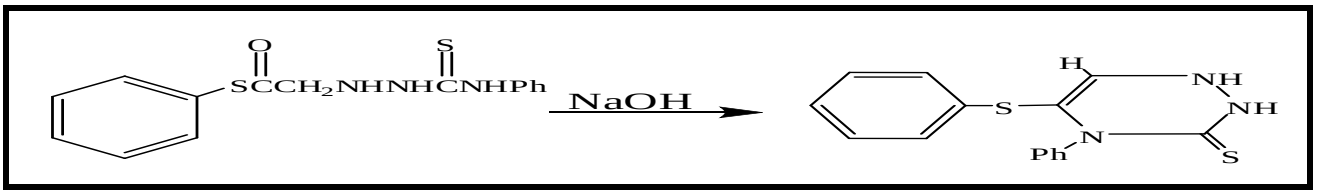
Compound [B] react with isothiophenylcynate under nucleophilic condition to prepare anew derivative [20] compound as shown in Equation (3.8). Physical properties of compound (20) are listed in Table (1). FT-IR spectrum of compound [20] showed the appearance of characteristic bands at (3415, 3213) cm^{-1} belong to ν (NH) group and appearance of new band at (1191) cm^{-1} belong to ν(C=S), other band at (1612) cm^{-1} due to ν(C=O). All other details of FT-IR spectral data of compound (20) are listed in Table (2) and Figure (15). ^{1}HNMR, ^{13}C-NMR sees in Tables (3), (4) and Figures (9, 10).



Equation

Synthesis S-(4-phenyl-1, 2, 4-triazine-3-thion) thiophenol [21]

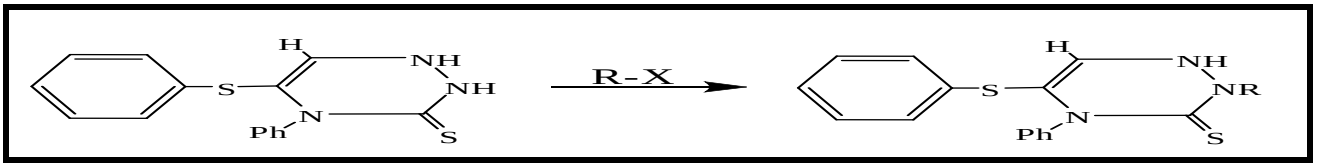
The treatment of compound [20] with NaOH affords intramolecular cyclization to give [21] compound as shown in Equation (3.9). Physical properties of compound (21) are listed in Table (1). FT-IR spectrum of compound [21] showed the disappearance of absorption bands at (1612) cm^{-1} belong to ν(C=O), (2943) cm^{-1} belong to ν(C-H) aliphatic and band appearance at (1579) cm^{-1} belong to ν(C=C) alkene and (1315) cm^{-1} belong to ν(C=S). All other details of FT-IR spectral data of compound (21) are listed in Table (2) and ^{1}HNMR spectral data sees in Table (3).



Equation

Synthesis of S-(4-phenyl-2-N-substituted-1,2,4-triazin-3-thion) thiophenol [22, 23]

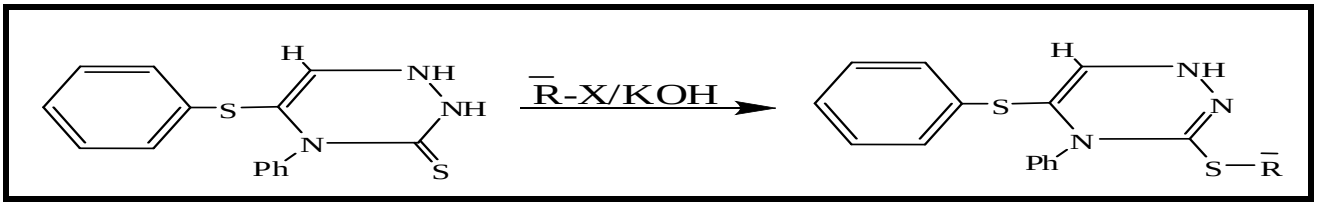
The cyclic product [21] treated to prepare other derivatives [22, 23] by reaction with different alkyl halides as shown in Equation (3.10). Physical properties of compounds (22, 23) are listed in Table (1). FT-IR spectrum of compounds [22, 23] showed the appearance of characteristic bands at (3380, 3361) cm^{-1} belong to ν(N-H), (2927, 2941) cm^{-1} belong to ν(C-H) aliphatic and (1311, 1307) cm^{-1} belong to ν(C=S). All other details of FT-IR spectral data of compounds (22, 23) are listed in Table (2).



Equation

Synthesis of S-(4-phenyl-1, 2, 4-triazine-3-substituted) thiophenol [24-26]

Another new derivative [24-26] was prepared by treatment of compound [21] with different alkyl halides mechanism type of this reaction called S_N2 as shown in Equation (3.11). Physical properties of compounds (24-26) are listed in Table (1). FT-IR spectrum of compounds [24-26] showed the appearance of characteristic bands at (3386- 3072) cm^{-1} due to ν(N-H), (1627-1600) cm^{-1} due to ν(C=N), (1591-1583) cm^{-1} due to ν(C=C). All other details of FT-IR spectral data of compounds (24-26) are listed in Table (2) and ^{1}HNMR spectral data of compound (25) sees in Table (3).



Equation

Biological Activity

In Gram positive bacteria, the adsorption is occurring in the lipoteichoic acid layer which is characterized by the charged nature and the ability to interact with the molecules. On the other hand in the gram-negative bacteria, the lipid layer (highly nonpolar layer) is the target of the biocide molecules. The adsorption disturbs the selective permeability of these membranes, and causes a severe disturbance of the biological reaction inside the cells due to the diffusion of several compounds from the environment due to the absence of the selective permeability [17, 18].

Escherichia coli was inactive inhibited by the compounds [B, 13, 14, 21 and 15] and showed slightly inhibition in compounds [20, 19, 22 and 25] showed highly inhibition in compound [2].

Staphylococcus aurus was inactive inhibited by the compounds [B, 2, 13, 20, 14, 21, 16, 19, 22 and 25].

Klebsiella pneumonia was inactive inhibited by the compounds [B, 2, 13, 20, 21 and 22] and showed slightly inhibition in compounds [16 and 25] while in compounds [14 and 19] showed highly inhibition.

Staphylococcus epidermidis was inactive inhibited by the compounds [B, 13, 21, 16, 22 and 25] and showed slightly inhibition in compound [14] while in compounds [2 and 19] showed moderately inhibition and highly inhibition in compound [20].

The anti-fungal activity for ***Aspergillus*** was inhibited by the compounds [B, 13 and 20] as showed in Table (6).

Conclusion

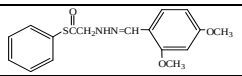
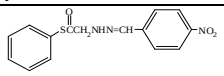
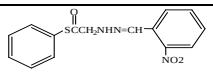
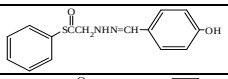
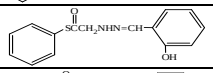
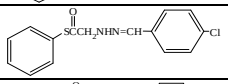
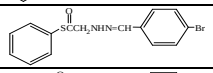
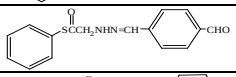
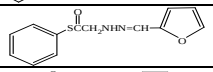
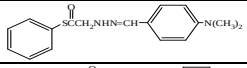
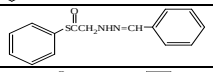
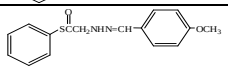
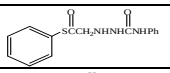
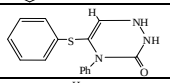
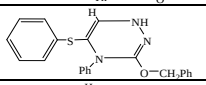
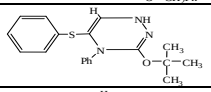
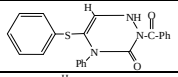
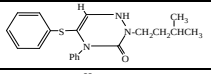
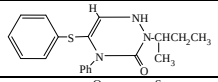
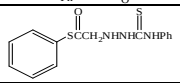
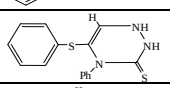
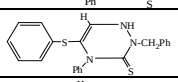
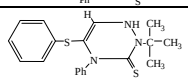
In this work we report the synthesis of new heterocyclic and Schiff base derivatives from thiophenol compound as starting material. The FT-IR, ^{1}H-NMR and ^{13}C-HNMR data for some of them gave a good indication for the formation of the prepared derivatives and the biological activity of some compounds Ranging between highly to Slightly inhibition.

Table 1: The physical properties of compounds [1-26]

Comp. No.	Chemical formula	(M.Wt.)	M.P. (C°)	Color	Yield (%)
1	$C_{17}H_{18}N_2O_3S$	330	136-138	Off white	64
2	$C_{15}H_{13}N_3O_3S$	315	10-112	Yellow	84
3	$C_{15}H_{13}N_3O_3S$	315	86-88	Dark yellow	60
4	$C_{15}H_{14}N_2O_2S$	286	72-74	Green-Yellow	65
5	$C_{15}H_{14}N_2O_2S$	286	126-128	White	60
6	$C_{15}H_{13}ClN_2OS$	304	26-28	Off white	68
7	$C_{15}H_{13}BrN_2OS$	349	127-129	Orang	64
8	$C_{16}H_{14}N_2O_2S$	298	210-211	Yellow	83
9	$C_{13}H_{12}N_2O_2S$	260	90-92	Light green	61
10	$C_{17}H_{19}N_3OS$	313	150-152	Red-Brown	74
11	$C_{15}H_{14}N_2OS$	270	88-90	Brown	73
12	$C_{16}H_{16}N_2O_2S$	300	124-126	Yellow	68
13	$C_{15}H_{15}N_3O_2S$	301	122-124	Off white	81
14	$C_{15}H_{13}N_3OS$	283	150-153	Light orang	74
15	$C_{22}H_{19}N_3OS$	373	210-211	Pale yellow	63
16	$C_{19}H_{21}N_3OS$	339	269-271	Dark brown	71

17	$C_{22}H_{17}N_3O_2S$	387	110-113	Brown	71
18	$C_{20}H_{23}N_3OS$	353	180-183	Dark yellow	63
19	$C_{19}H_{21}N_3OS$	339	221-223	Light yellow	69
20	$C_{15}H_{15}N_3OS_2$	317	158-160	Light yellow	90
21	$C_{15}H_{13}N_3OS_2$	299	171-173	Off white	79
22	$C_{22}H_{19}N_3S_2$	389	200-202	Pale yellow	70
23	$C_{19}H_{21}N_3S_2$	355	230-232	Brown	62
24	$C_{22}H_{17}N_3OS_2$	403	104-106	brown	75
25	$C_{19}H_{21}N_3OS_2$	369	150-152	Yellow	61
26	$C_{19}H_{21}N_3OS_2$	355	192-194	Dark yellow	68

Table 2: FT-IR spectral data (cm^{-1}) of compounds [1-26]

Comp. No.	Structure	FT-IR Spectral data, cm^{-1}
1		v(N-H)= 3409, v(C=O)= 1654, v(C-N)= 1602, v(C-O)= asym. (1278) sym. (1029) v(C-H) aliph.= (3056-2964).
2		v(N-H)= 3417, v(C=O)= 1674, v(C=N)= 1616, v(NO_2)= asym. (1525) sym. (1352).
3		v(N-H)= 3415, v(C=O)= 1697, v(C=N)= 1668, v(NO_2)= asym. (1525) sym. (1355).
4		v(N-H)= 3415, v(C=O)= 1652, v(C=N)= 1608, v(O-H)= 3477.
5		v(N-H)= 3390, v(C=O)= 1670, v(C=N)= 1620, v(O-H)= 3487.
6		v(N-H)= 3413, v(C=O)= 1633, v(C=N)= 1616, v(C-Cl)= 663.
7		v(N-H)= 3411, v(C=O)= 1664, v(C=N)= 1606, v(C-Br)= 516.
8		v(N-H)= 3413, v(C=O)= 1662, v(C=N)= 1620, v(C-H) ald.= 2939, v(C=O) ald.= 1701.
9		v(N-H)= 3425, v(C=O)= 1672, v(C=N)= 1581, v(C-O)= 1211, v(C=C)= 1510, 1479.
10		v(N-H)= 3413, v(C=O)= 1664, v(C=N)= 1612, v(C-N)= 1178.
11		v(N-H)= 3436, v(C=O)= 1670, v(C=N)= 1616, v(C=C) arom.= 1579, 1481.
12		v(N-H)= 3431, v(C=O)= 1668, v(C=N)= 1602, v(C-O)= asym. (1251) sym. (1027), (C-H) aliph.= 2954, 2839.
13		v(N-H)= 3203, 3313, v(C=O) thioester=1704, v(C=O) amide= 1672, v(C-H) aliph.= 2908.
14		v(N-H)= 3382, 3402, v(C=O) amide(I)= 1618, v(C=C) alkene=1602.
15		v(N-H)= 3386, v(C=N)= 1627, v(C=C) alkene=1598, v(C-H) arom.= 3064
16		v(N-H)= 3367, v(C=N)= 1672, v(C=C) alkene=1641, v(C-H) aliph.= 2842,2802.
17		v(N-H)= 3068, v(C=O) amide= 1602, v(C=C) alkene=1581, v(C-H) arom.= 3006
18		v(N-H)= 3415, v(C=O) amide= 1627, v(C=C) alkene=1595, v(C-H) aliph.= 2966-2898.
19		v(N-H)= 3409, v(C=O) amide= 1620, v(C=C) alkene=1587, v(C-H) aliph.= 2962-2813.
20		v(N-H)= 3415, 3213, v(C=O) thioester=1612, v(C=S) = 1191, v(C-H) aliph.= 2943.
21		v(N-H)= 3380, 3344, v(C=C) alkene=1579.
22		v(N-H)= 3380, v(C=C) alkene=1618, v(C=S) = 1311, v(C-H) arom.= 3056, aliph. 2927.
23		v(N-H)= 3361, 3213, v(C=C) alkene =1649, v(C=S) = 1307, v(C-H) aliph.= 2941, 2835.

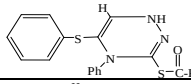
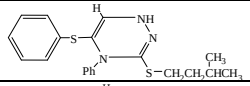
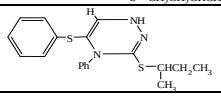
24		v(N-H)= 3072, v(C=N)= 1600, v(C=C) alkene=1583, v(C-H) arom. =3014.
25		v(N-H)= 3353, v(C=N)= 1627, v(C=C) alkene=1591, v(C-H) aliph.= 2972, 2937.
26		v(N-H)= 3386, v(C=N)= 1618, v(C=C) alkene=1585, v(C-H) aliph.= 2962, 2813.

Table 3: ^{1}H-NMR spectral data (δ ppm) for some compounds

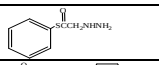
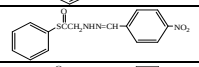
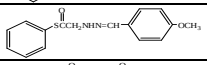
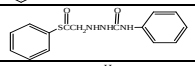
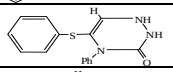
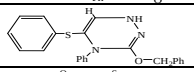
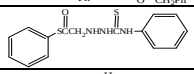
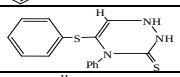
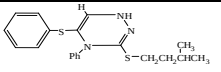
Comp. No.	Structure	^{1}H-NMR spectral data (δ ppm)
B		3.55 (s, 2H, NH_2 protons), 3.76 (s, 2H, (C=O)-C<u>H</u>$_2$), (7.14-7.35) (m, 5H, Ar-<u>H</u>), 7.62 (s, 1H, (CH_2-N<u>H</u>-NH_2).
2		3.78 (s, 2H, (C=O)-C<u>H</u>$_2$), (7.14-7.78) (m, 9H, Ar-<u>H</u>), 8.28 (s, 1H, CH_2-N<u>H</u>-NH_2), 8.88 (s, 1H, N=C<u>H</u>).
12		3.72 (s, 2H, (C=O)-C<u>H</u>$_2$), 4.09 (s, 1H, Ph-O-C<u>H</u>$_3$), (6.94-7.90) (m, 9H, Ar-<u>H</u>), 8.09 (s, 1H, N=C<u>H</u>), 8.60 (s, 1H, CH_2-N<u>H</u>-NH_2).
13		3.77 (s, 2H, (C=O)-C<u>H</u>$_2$), (6.90-7.48) (m, 10H, Ar-<u>H</u>), 8.08 (s, 1H, CH_2-N<u>H</u>), 8.88 (s, 1H, N<u>H</u>-(C=O)), 9.58 (s, 1H, (C=O)-N<u>H</u>-Ph).
14		4.09 (s, 1H, (C=C-<u>H</u>)), (7.16-7.29) (m, 5H, Ar-<u>H</u>), 8.36 (s, 1H, (=C-N<u>H</u>)), 8.46 (s, 1H, N<u>H</u>-(C=O)).
15		3.32 (s, 2H, O-C<u>H</u>$_2$-Ph), 4.65 (s, 1H, (C=C-<u>H</u>), (7.01-7.56) (m, 15H, Ar-<u>H</u>), 8.47 (s, 1H, (=C-N<u>H</u>).
20		3.76 (s, 2H, (C=O)-C<u>H</u>$_2$), (7.09-7.30) (m, 10H, Ar-<u>H</u>), 7.54 (s, 1H, (CH_2-N<u>H</u>), 9.68 (s, 1H, N<u>H</u>-(C=S)), 10.26 (s, 1H, ((C=S)-N<u>H</u>-Ph).
21		4.21 (s, 1H, (C=C-<u>H</u>)), (7.02-7.29) (m, 5H, Ar-<u>H</u>), 8.46 (s, 1H, (=C-N<u>H</u>)), 10.43 (s, 1H, N<u>H</u>-(C=S)).
25		0.82 (d, 6H, CH-(C<u>H</u>$_3$)$_2$), 1.24 (q, 2H, CH_2-C<u>H</u>$_2$-CH), 1.60 (m, 1H, CH_2-C<u>H</u>-(CH_3)$_2$), 3.10 (t, 2H, S-C<u>H</u>$_2$), 4.46 (s, 1H, C=C-<u>H</u>), (6.80-7.56), (m, 5H, Ar-<u>H</u>), 8.51 (s, 1H, (=C-N<u>H</u>).

Table 4: ^{13}C-NMR spectral data (δ ppm) for some compounds

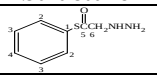
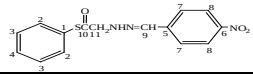
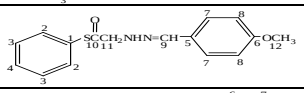
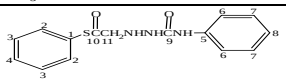
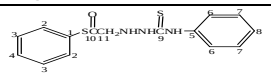
Comp. No.	Structure	^{13}C-NMR spectral data (δ ppm)
B		40.56 (C6), 129.46-129.56 (C1,C3), 130.84 (C4), 136.44 (C2), 171.91 (C5).
2		40.32 (C11), 121.54 (C8), 129.51 (C1,C3), 130.45-131.48 (C4,C7), 134.98 (C2,C5), 141.61 (C9), 145.14 (C6), 170.87 (C10).
12		40.33 (C11), 55.83 (C12), 114.84 (C8), 129.26-129.58 (C1,C3,C7), 130.03130.53 (C2,C4,C5), 143.77 (C9), 161.04 (C6), 170.30 (C10).
13		44.43 (C11), 118.70 (C6), 128.29 (C8), 129.07-129.99 (C1,C3,C4,C7), 136.28 (C2), 139.79 (C5), 154.10 (C9), 171.15 (C10).
20		44.44 (C11), 122.00 (C6), 126.43 (C8), 128.92 (C7), 129.52-129.57 (C1,C3), 130.29 (C4), 136.27 (C2), 139.79 (C5), 169.81 (C9), 171.14 (C10).

Table 5: Anti-bacteria activity for some prepared compounds

Comp. No.	Inhibition zone at (0.02g/ml.) after 24 hrs., (mm)			
	Escherichia coli	***Staphylococcus aurus***	***Klebsiella pneumonia***	***Staphylococcus epidermidis***
C	-	-	-	-
B	-	-	-	-
2	15	-	-	11
13	-	-	-	-
20	9	-	-	13
14	-	-	16	8
21	-	-	-	-
16	-	-	9	-
19	8	-	13	10
22	8	-	-	-
25	9	-	9	-

- Solvent: DMSO
- Zone inhibition:

1. (-) Inactive inhibition zone < 6 mm.
2. Slightly inhibition zone 6-9 mm.
3. Moderately inhibition zone 10-12 mm.
4. Highly inhibition zone 13-17 mm.

Table 6: Anti-fungal activity for compounds [B, 13 and 20]

Comp. No.	Inhibition zone at (0.003g/ml.) after 24 hrs., (mm)
	Aspergillus
C	39
B	31
13	36
20	33

- Solvent: DMSO
- Control: Amoxicillin

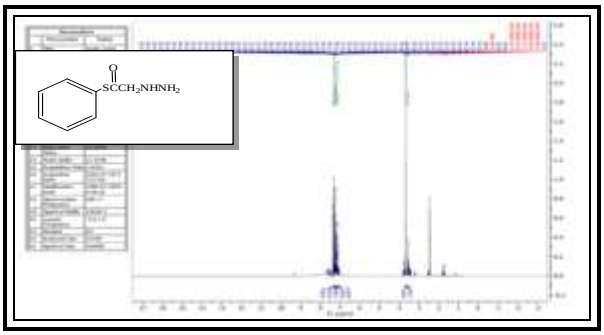


Figure 1: ^{1}H-NMR spectrum of compound [B]

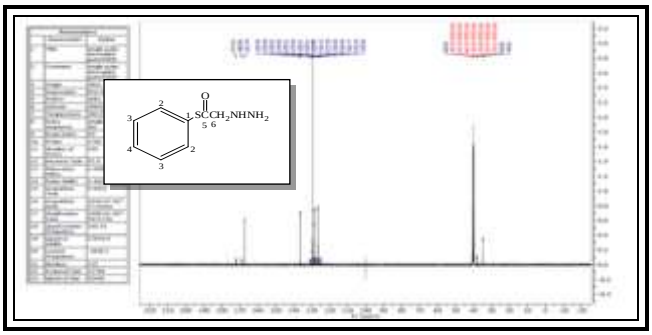


Figure 2: ^{13}C-NMR spectrum of compound [B]

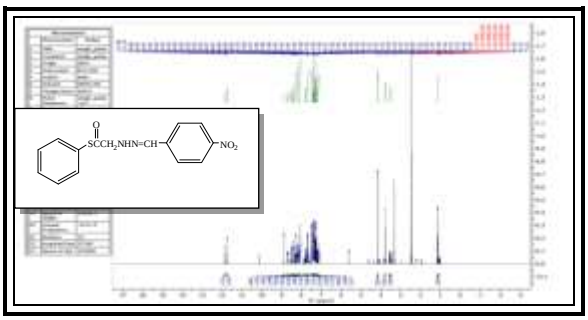


Figure 3: ^{1}H-NMR spectrum of compound [2]

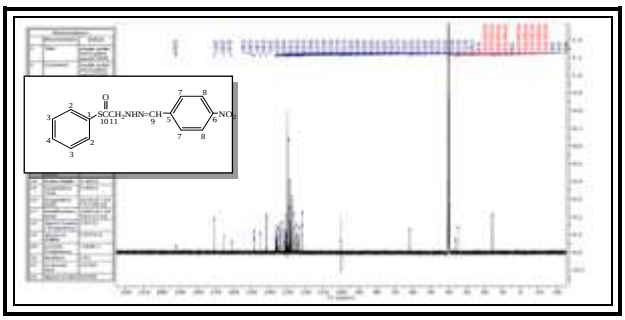


Figure 4: ^{13}C-NMR spectrum of compound [2]

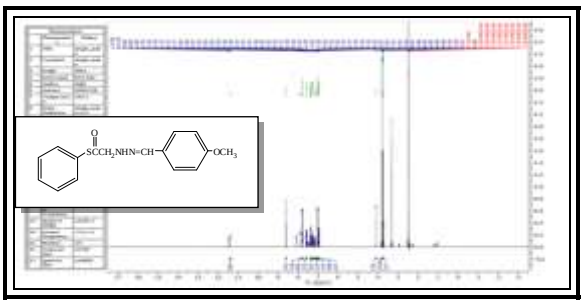


Figure 5: ^{1}H-NMR spectrum of compound [12]

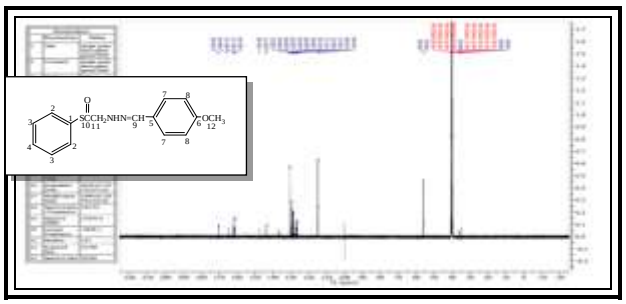


Figure 6: ^{13}C-NMR spectrum of compound [12]

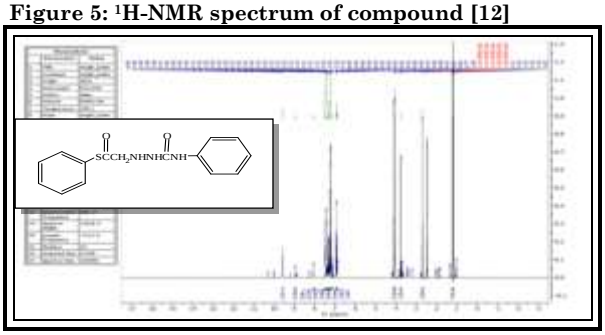


Figure 7: ^{1}H-NMR spectrum of compound [13]

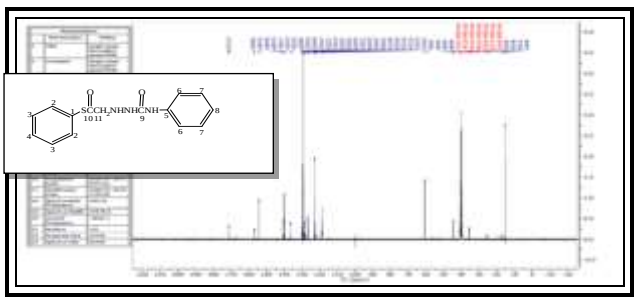


Figure 8: ^{13}C-NMR spectrum of compound [13]

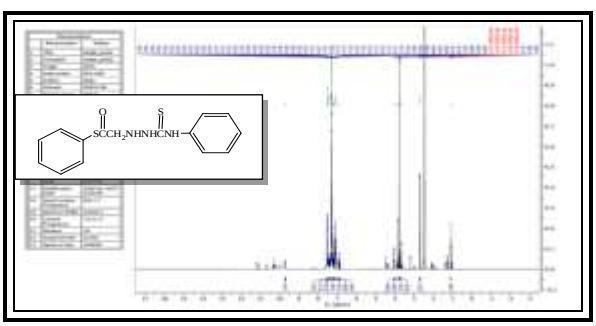


Figure 9: ^{1}H-NMR spectrum of compound [20]

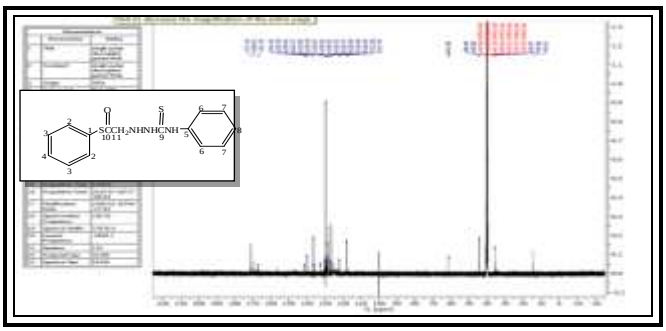


Figure 10: ^{13}C-NMR spectrum of compound [20]

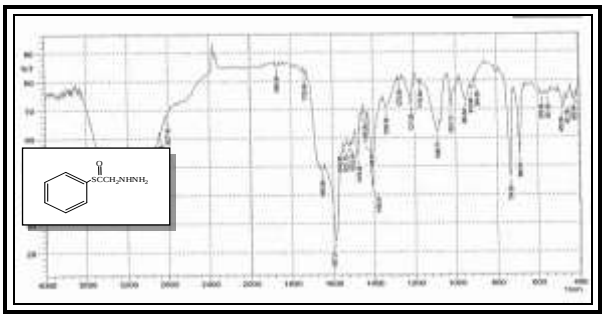


Figure 11: FT-IR spectrum of compound [B]

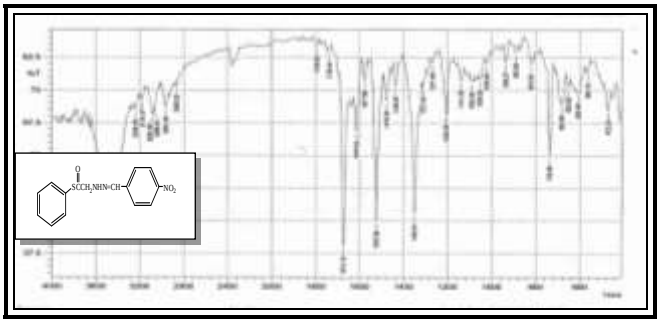


Figure 12: FT-IR spectrum of compound [2]

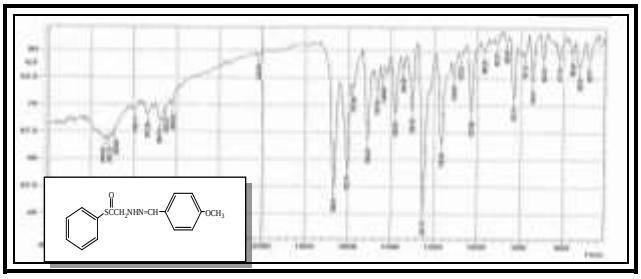


Figure 13: FT-IR spectrum of compound [12]

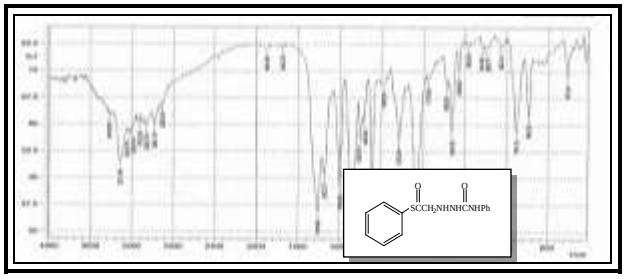


Figure 14: FT-IR spectrum of compound [13]

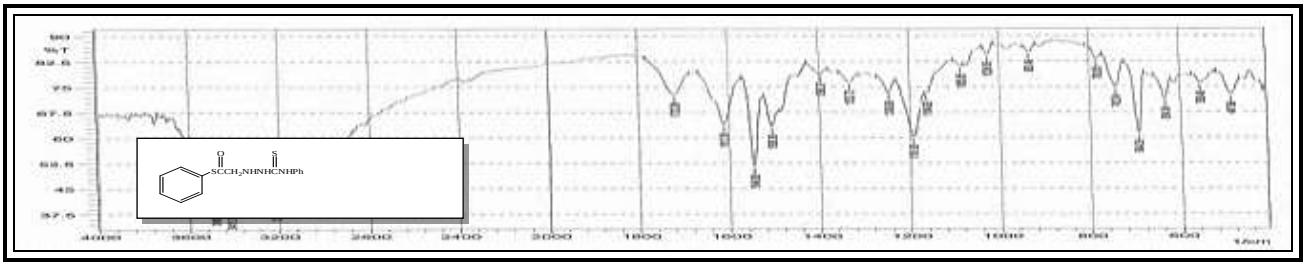


Figure 15: FT-IR spectrum of compound [20]

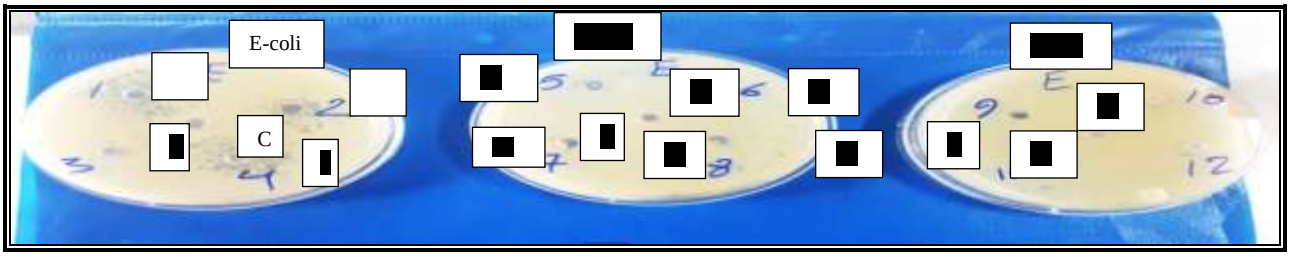


Figure 16: Effect of compounds [B, 2, 13, 20, 14, 21, 16, 19, 22 and 25] on *Escherichia coli*

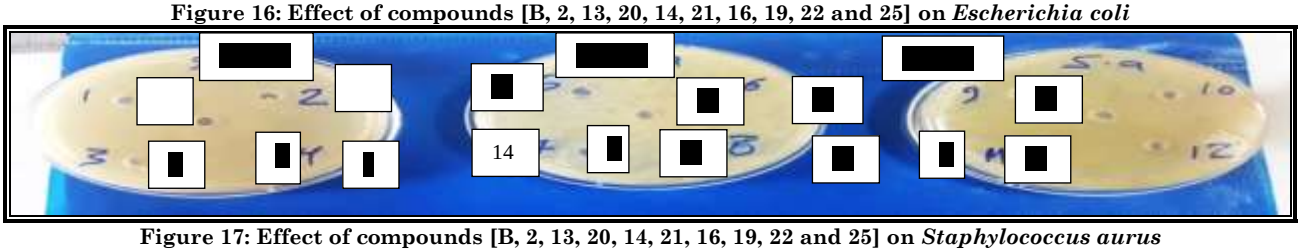


Figure 17: Effect of compounds [B, 2, 13, 20, 14, 21, 16, 19, 22 and 25] on *Staphylococcus aurus*

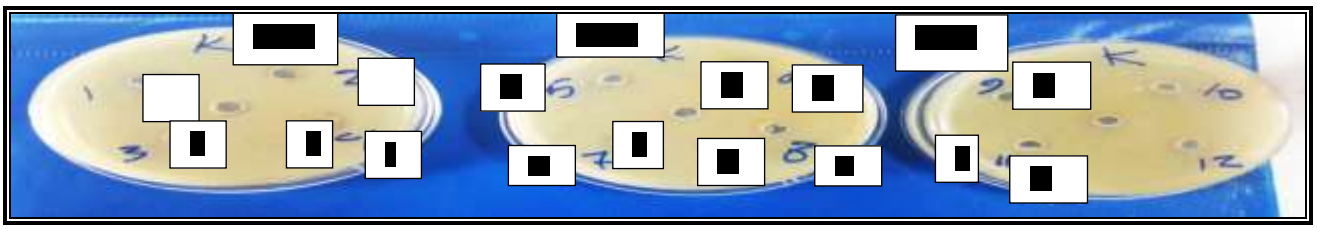


Figure 18: Effect of compounds [B, 2, 13, 20, 14, 21, 16, 19, 22 and 25] on *Klebsiella pneumonia*

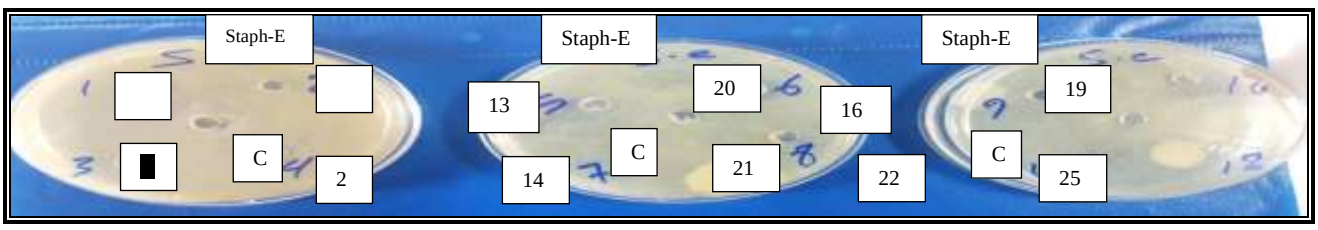
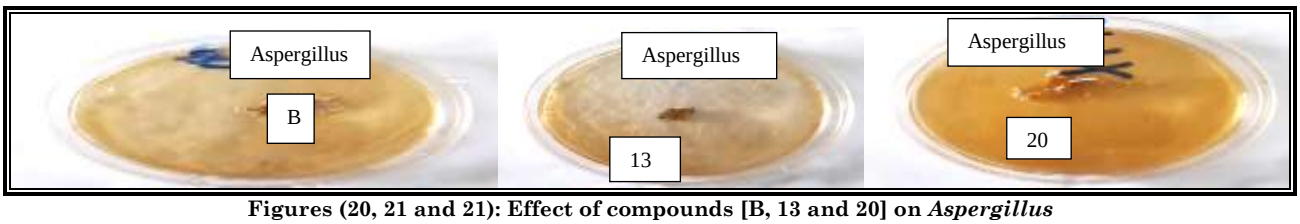


Figure 19: Effect of compounds [B, 2, 13, 20, 14, 21, 16, 19, 22 and 25] on *Staphylococcus epidermidis.*



Figures (20, 21 and 21): Effect of compounds [B, 13 and 20] on *Aspergillus*

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